EFFECT OF INTENSIFIED STRESS-PROTECTIVE THERAPY ON THE CIRCADIAN RHYTHM OF MEAN ARTERIAL PRESSURE IN CHILDREN OVER 7 YEARS OF AGE WITH SEVERE COMBINED TRAUMATIC BRAIN INJURY

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Abstract. *This study evaluated the effect of intensified stress-protective therapy on the circadian rhythm of mean arterial pressure (MAP) in 20 children aged 7–18 years with severe combined traumatic brain injury. Group 1 included 10 patients treated during 2018–2022, and Group 2 included 10 patients treated during 2023–2024. MAP circadian rhythm was assessed by mesor, acrophase, bathyphase, amplitude, and daily fluctuation range. The mesor was 84±1 mmHg in Group 1 and 80±2 mmHg in Group 2; amplitude was 7±2 and 10±4 mmHg, respectively, while the daily fluctuation range was 14±4 and 20±8 mmHg. No significant intergroup differences were found in the main phase characteristics. Circadian rhythm inversion persisted for 35% and 42% of the intensive care period, respectively. MAP showed strong positive correlations with both systolic and diastolic blood pressure. Despite greater injury severity in Group 2, MAP remained predominantly within the physiological range, suggesting preservation of compensatory-adaptive hemodynamic mechanisms during intensified stress-protective therapy.*

Keywords: *severe combined traumatic brain injury, children, mean arterial pressure, circadian rhythm, stress-protective therapy, mesor, acrophase, bathyphase, circadian rhythm inversion, hemodynamics, intensive care.*

Relevance. Severe combined traumatic brain injury (SCTBI) in children is associated with impaired cerebral perfusion, systemic hemodynamic disturbances, autonomic dysfunction, and a high risk of secondary brain injury. Current guidelines emphasize maintaining adequate arterial pressure and cerebral perfusion, preventing hypotension, and using continuous physiological monitoring [1, 2]. Brain–heart interactions may additionally affect heart rate, arterial pressure, autonomic

regulation, and myocardial function [3]. Therefore, hemodynamic assessment should include not only isolated blood pressure values but also their dynamic changes over time. Individualized hemodynamic management is especially important because mean daily arterial pressure may not fully reflect time-dependent cardiovascular disturbances [4]. Circadian rhythms are often disrupted in critically ill patients [5], and circadian characteristics may have clinical and prognostic significance in traumatic brain injury [6]. In addition, sedative and stress-protective therapy can modify systemic hemodynamic and metabolic responses [7].

Therefore, evaluation of mean arterial pressure (MAP) in children with SCTBI should include not only its absolute values but also its circadian organization, including the mesor, acrophase, bathyphase, amplitude, and daily range of fluctuations. The present study compares children aged 7–18 years treated during 2018–2022 with those treated during 2023–2024 under an intensified stress-protective regimen, thereby allowing assessment of the relationship between treatment strategy and circadian hemodynamic adaptation.

Objective. To investigate and comparatively assess the effect of intensified stress-protective pharmacological therapy on the circadian rhythm of mean arterial pressure (MAP) during the acute period of severe combined traumatic brain injury in children older than 7 years.

Materials and Methods. The study included 20 children aged 7–18 years who were treated for severe combined traumatic brain injury. Group 1 comprised 10 patients treated during 2018–2022, while Group 2 included 10 patients treated during 2023–2024. The groups were comparable in terms of diagnosis, age, and overall clinical condition. Injury severity was assessed using the Injury Severity Score (ISS) and the Glasgow Coma Scale. The mean ISS score was 23,1±5,72 points in Group 1 and 29,8±4,0 points in Group 2, indicating a tendency toward more severe injury in Group 2. All patients received comprehensive treatment in the intensive care unit. During the first 10 days after injury, central venous pressure, peripheral oxygen saturation (SpO_2), heart rate, and MAP were recorded hourly. Central and peripheral hemodynamic parameters were also assessed. The circadian rhythm of MAP was evaluated according to its mesor, acrophase, bathyphase, amplitude, and daily range of fluctuations. Statistical analysis was performed using methods of variation statistics. Mean values and standard errors were calculated, intergroup differences were assessed using Student’s t-test, and relationships between variables were evaluated using paired correlation analysis. A p-value of <0.05 was considered statistically significant.

Results. The mean phase characteristics of the circadian rhythm of MAP did not differ significantly between the two groups. The mesor was 84±1 mmHg in Group 1 and 80±2 mmHg in Group 2. Acrophase values were 90±4 and 91±7 mmHg, respectively, while bathyphase values were 77±5 and 71±5 mmHg. The circadian rhythm amplitude was 7±2 mmHg in Group 1 and 10±4 mmHg in Group 2, while the daily fluctuation range was 14±4 and 20±8 mmHg, respectively. On the first day of observation, the MAP circadian mesor remained within the age-appropriate physiological range in both groups, measuring 83±4 mmHg in Group 1 and 73±7 mmHg in Group 2. During subsequent observation, the mesor remained relatively stable in Group 1, whereas a slight upward trend was noted in Group 2 after day 20. The mean circadian rhythm of MAP in both groups was characterized by wave-like, nearly synchronous fluctuations. The acrophase occurred at approximately 20:00 in Group 1 and 18:00 in Group 2. The amplitude and daily range of MAP fluctuations tended to be greater in Group 2 than in Group 1 on days 1, 10, 21, and 24. Circadian rhythm inversion of MAP persisted for 35% of the intensive care period in Group 1 and 42% in Group 2. Correlation analysis demonstrated a strong positive relationship between MAP and diastolic blood pressure in both groups, with correlation coefficients of r=0.71 in Group 1 and r=0.92 in Group 2. The association between MAP and systolic blood pressure was even stronger, reaching r=0.94 and r=0.96, respectively. These findings suggest that sedative and stress-protective intensive therapy did not substantially alter the functional relationship between the major hemodynamic parameters. The MAP response to hyperthermia was weaker in Group 2 than in Group 1, with correlation coefficients of r=0.15 and r=0.51, respectively. A negative correlation trend between anti-inflammatory therapy and MAP was observed in both groups: r=−0.55 in Group 1 and r=−0.43 in Group 2. In Group 2, positive correlations were also identified between MAP and the administration of vasodilators, nootropic agents, and vitamins, with correlation coefficients of r=0.54, r=0.63, and r=0.64, respectively. The identified correlations suggest comparatively more active compensatory mechanisms in Group 2. Despite a tendency toward more severe injury, these patients demonstrated preserved adaptive reserves and a more pronounced compensatory hemodynamic response during intensified stress-protective therapy.

Conclusion. In children older than 7 years with severe combined traumatic brain injury, the circadian mesor of MAP remained predominantly within the physiological range during both the initial and subsequent days of observation. No significant intergroup differences were identified in the main phase characteristics

of the MAP circadian rhythm. However, Group 2 demonstrated a tendency toward greater circadian amplitude and daily fluctuations, as well as a slightly longer duration of circadian rhythm inversion. The strong correlations of MAP with systolic and diastolic blood pressure, together with the specific responses to hyperthermia and pharmacological therapy, indicate comparatively active compensatory-adaptive mechanisms in Group 2. These findings suggest that intensified stress-protective therapy may contribute to maintaining hemodynamic stability and adaptive responses in children with severe combined traumatic brain injury.

REFERENCES

1. Kochanek P.M., Tasker R.C., Carney N., et al. Guidelines for the management of pediatric severe traumatic brain injury: update of the Brain Trauma Foundation guidelines // Pediatric Critical Care Medicine. – 2019. – Vol. 20, No. 3S. – P. 71–82. – DOI: 10.1097/PCC.0000000000001735.

2. Kochanek P.M., Tasker R.C., Bell M.J., et al. Management of pediatric severe traumatic brain injury: 2019 consensus and guidelines-based algorithm for first and second tier therapies // Pediatric Critical Care Medicine. – 2019. – Vol. 20, No. 3. – P. 269–279.

3. El-Menyar A., Goyal A., Latifi R., et al. Brain-heart interactions in traumatic brain injury // Cardiology in Review. – 2017. – Vol. 25, No. 6. – P.

4. Di Filippo S., Messina A., Pelosi P., et al. Eight rules for the haemodynamic management of traumatic brain-injured patients // European Journal of Anaesthesiology and Intensive Care. – 2023. – Vol. 2, No. 4. – P. 29–35. – DOI: 10.1097/EA9.0000000000000029.

5. Felten M., Dame C., Lachmann G., et al. Circadian rhythm disruption in critically ill patients // Acta Physiologica. – 2023. – Vol. 238, No. 1. – DOI: 10.1111/apha.13962.

6. Kuo L.-T., Lu H.-Y., Huang A.P.-H. Prognostic Value of Circadian Rhythm of Brain Temperature in Traumatic Brain Injury // Journal of Personalized Medicine. – 2021. – Vol. 11, No. 7. – Article 620. – DOI: 10.3390/jpm11070620.

7. Kurni M., Kaloria N., Hazarika A., et al. Comparison of Midazolam and Propofol Infusion to Suppress Stress Response in Patients With Severe Traumatic Brain Injury: A Prospective, Randomized Controlled Trial // Korean Journal of Neurotrauma. – 2023. – Vol. 19, No. 1. – P. 70–81. – DOI: 10.13004/kjnt.2023.19.e4.