

Circadian rhythm of general peripheral vascular resistance in acute concomitant severe traumatic brain injury

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Abstract

In the first 25 days, the GPVR circadian rhythm mesor was increased in all groups of patients with CSTBI. The GPVR circadian rhythm consisted mainly of ultradian 3-4 hour oscillations in all patients. From 9 to 17 days, the GPVR indicators in the circadian rhythm in group 3 were higher than in the first and second groups by 13%. In the 1st group on the second week of the study there was an inversion of the circadian rhythm GPVR, in the 2nd group at 14:00, and in the 3rd group at 13:00. In group 1, 7, 5, 4, 4, 5 daytime waves of changes in the amplitude of the GPVR circadian rhythm were quite distinguishable. In group 2 there are 4, 5, 6, 5, 5 daily fluctuations. In group 3 there are 6,4,6,6,4 daily fluctuations. For 25 days after the injury, the tendency to the hypercirculatory type of blood circulation persisted in all age groups.

Keywords: circadian rhythm, total peripheral vascular resistance, combined severe traumatic brain injury.

Relevance. The frequency and severity of craniocerebral injuries, high mortality (up to 26.8-81.5%) determine the urgency of this problem and require further development of methods for treating TBI and its complications. TBI is more common between the ages of 20 and 50, that is, during the period of greatest working capacity, 1.5 times more often in men than in women. The TBI problem has social, economic and defense implications. In about 50% of cases, there is a combination of STBI with systemic trauma of varying severity. Currently, mortality with combined STBI reaches 80%, and among survivors - up to 75% of victims remain with severe neurological defects. At present, the opinion of all leading specialists in the field of neurotrauma boils down to the following basic concept: brain damage in STBI is determined not only by the primary impact at the moment of injury, but also by the action of various damaging factors during the next hours and days, the so-called factors of secondary brain damage (SBD), on which the clinical prognosis and outcome of the acute and long-term periods after STBI depend. In this

regard, the main task of providing care for STBI at the stage of hospitalization of patients is to prevent SBD [1-5].

Purpose of the work. To study the circadian rhythm of the total peripheral vascular resistance in acute concomitant severe traumatic brain injury.

Material and research methods. The indicators of a comprehensive examination of 30 patients with concomitant severe craniocerebral trauma (CSTBI) who were admitted to the ICU of the neurosurgical department of RSCEMA in the first hours after an accident - 28, catatrauma of 2 patients were studied. According to indications, 29 patients were started on admission to invasive mechanical respiratory support (MRS). Monitoring was carried out by complex hourly registration of parameters of body temperature, hemodynamics, respiration. Mechanical respiratory support was initiated with artificial lung ventilation (ALV) for a short time followed by switching to SIMV. The severity of the condition was assessed by scoring methods according to the scales for assessing the severity of combined injuries - the CRAMS scale, the assessment of the severity of injuries according to the ISS scale. On admission, impaired consciousness in 29 injured patients was assessed on the Glasgow Coma Scale (GS) 8 points or less. Patients were considered in three age groups: group 1 - 19-40 years old (13), group 2 - 41-60 years old (9), 3 - 61-84 years old (8 patients).

In 28 patients, the clinic was dominated by the diencephalic and mesencephalo-bulbar forms, which, due to a critical disorder of the vital systems (respiratory and cardiovascular), required urgent intensive therapy, and sometimes resuscitation.

Complex intensive care consisted in identifying and timely correction of deviations: MRS, after removing from shock pain-relieving, anti-inflammatory, antibacterial, infusion therapy, correction of protein and water-electrolyte balance disorders, surgical early correction to the extent possible, stress-protective therapy.

Result and discussion.

Table 1

Dynamics of the mesor of the circadian rhythm GPVR, in $\text{dyn}\cdot\text{c}\cdot\text{cm}^{-5}$.

Days	Group 1	Group 2	Group 3
1	1543±166	1344±171	1474±168
2	1440±58	1509±112	1588±78
3	1396±97	1513±128	1431±80
4	1455±66	1571±116	1582±138
5	1421±68	1415±101	1550±98
6	1417±69	1357±82	1542±67
7	1397±65	1384±106	1487±95
8	1388±74	1322±70	1434±91

9	1313±72	1301±54	1497±122
10	1365±90	1404±86	1560±134
11	1290±116	1281±95	1433±97
12	1193±71	1382±76	1434±154
13	1261±146	1298±77	1409±160
14	1372±81	1395±77	1479±111
15	1322±84	1343±99	1368±98
16	1300±108	1336±74	1523±150
17	1365±127	1285±75	1559±165
18	1427±111	1455±156	1404±132
19	1437±107	1367±116	1529±181
20	1398±129	1398±127	1596±172
21	1369±81	1190±114	1544±132
22	1237±92	1369±100	1591±232
23	1269±59	1270±127	1379±136
24	1234±90	1252±117	1577±165
25	1364±102	1376±124	1453±211

On the first day, the GPVR circadian rhythm mesor was increased in all groups of patients with CSTBI, remaining without significant dynamics during the first 25 days after severe trauma (table 1). The revealed tendency to an increase in the mesor of the circadian rhythm GPVR was an integral factor of the compensatory hemodynamic response aimed at increasing oxygen delivery to cellular structures, primarily the brain, due to the centralization of blood circulation and the effect of drug stress-protective therapy and urgent correction of the identified (functional, clinical and laboratory parameters) signs of violation of homeostasis systems. A more in-depth analysis made it possible to reveal some features in dynamics, age-related differences in structural changes in the circadian rhythms of GPVR.

Circadian rhythm GPVR from 1 to 8 days, dyn.c.cm^{-5} .

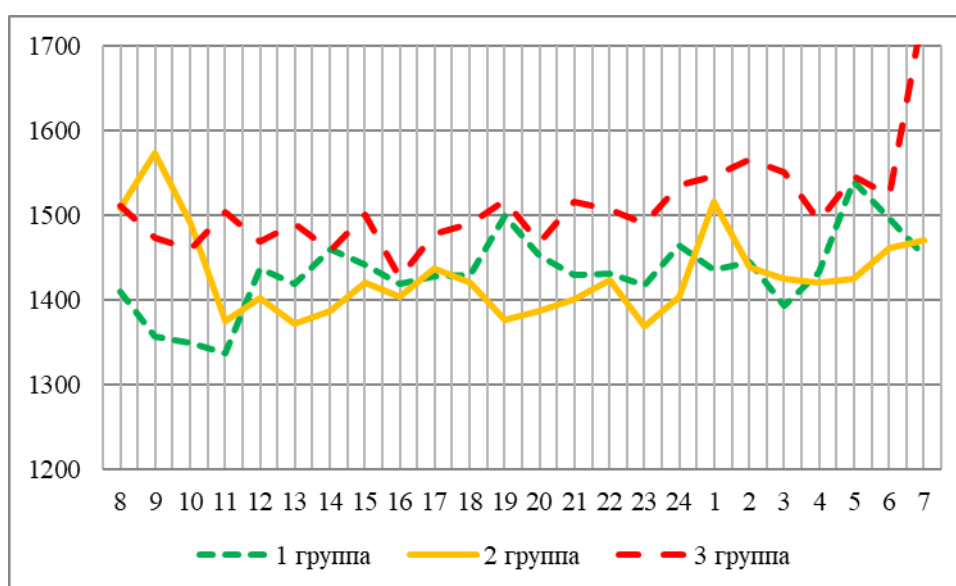


Fig.1

As shown in fig. 1, there were no significant differences in age groups in the first week after CSTBI. The GPVR circadian rhythm consisted mainly of ultradian 4 hour oscillations in all patients, in group 1 with acrophase at 9 am, in group 2 at 5 am, in group 3 at 7 am. That is, the normal projection of acrophase was detected only in injured young people (group 1). The average GPVR in group 3 (1511 ± 37) was significantly higher than in group 1 (1432 ± 31) and 2 (1430 ± 38) - by 5% ($p < 0.05$, respectively). Thus, in the 1st group in the acute period of CSTBI, despite the increased mesor of the circadian rhythm GPVR on days 1-8, there was a significant decrease in GPVR on average by 5%.

Circadian rhythm of GPVR from 9 to 17 days, in dyn.c.cm^{-5}

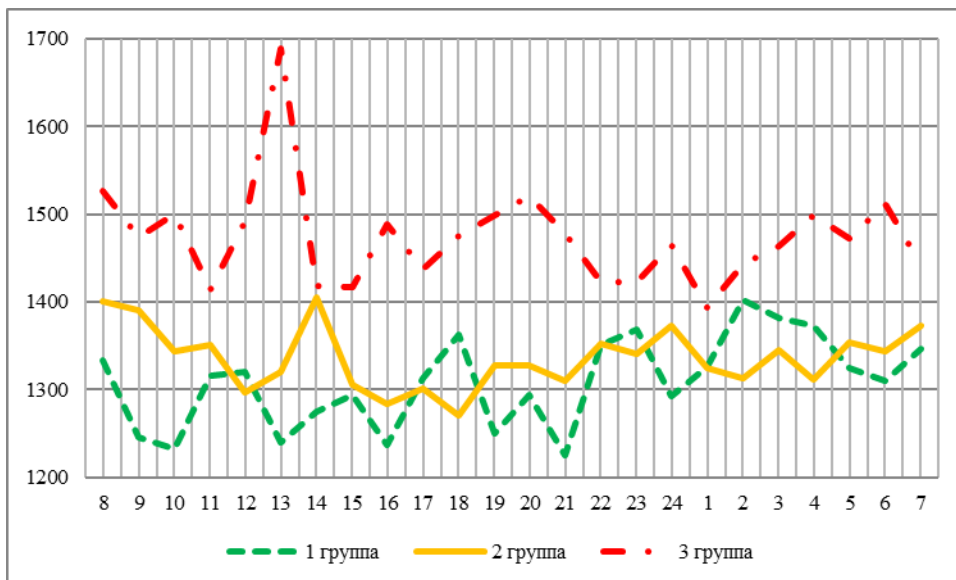


Fig.2

On days 9 - 17, the average daily GPVR curve in group 3 (1474 ± 39) was at a higher level than in groups 1 (1309 ± 42) and 2 (1335 ± 39). That is, the average GPVR values in the circadian rhythm for the period from 9 to 17 days in group 3 were higher than in the first and second groups by 13% ($p < 0.05$, respectively). The differences turned out to be significant at 13 o'clock in the afternoon, amounting to 36% ($p < 0.05$). Acrophase in group 1 in the second week of the study shifted to 2 am (inversion of the GPVR circadian rhythm occurred), in group 2 at 2 pm, and in group 3 at 1 pm. It should be noted that there was a tendency to decrease the period of ultradian oscillations to 3-4 hour waves, which was more pronounced in groups 1 and 2 (fig. 2).

Circadian rhythm GPVR from 18 to 25 days, in $\text{dyn}\cdot\text{cm}^{-5}$

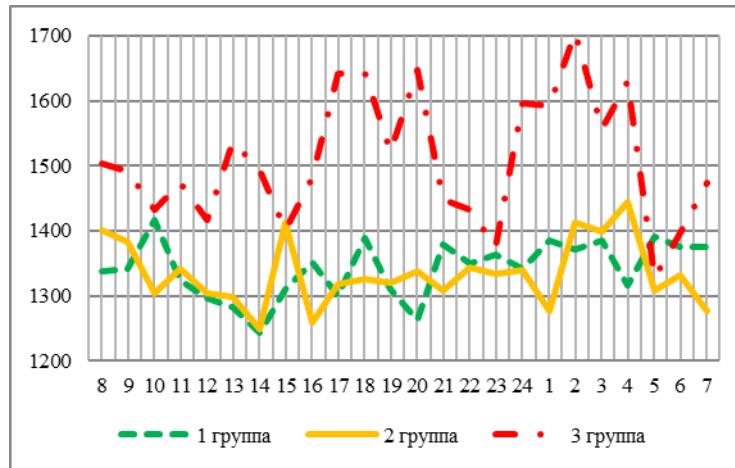


Fig.3

A significant difference on days 18 to 25 (fig. 3) was also found in patients of group 3, which was expressed in an increase in the amplitude of ultradian oscillations with the acrophase peak at 2 am by 24% ($p>0.05$), indicating a complete inversion of the circadian rhythm GPVR in patients over 61 years of age. In groups 1 and 2, 3-hour low-amplitude fluctuations prevailed, while in group 3 the amplitude of ultradian rhythms almost doubled, which characterized the pronounced instability of the peripheral vascular tone, more characteristic of the vasopressor effect of drug correction of hemodynamics in conditions of pituitary-adrenal insufficiency. Revealed repeated drops (about 5 times per day) GPVR created extremely unfavorable conditions for the work of the heart muscle, in general, significantly reducing the adaptive capabilities of the heart in conditions of damaging effects on cellular structures, the brain of numerous adverse factors (general intoxication, mitochondrial insufficiency, hypoxia, activation free radical oxidation and others), which inevitably leads to the development of multiple organ failure syndrome even in conditions of timely correction of homeostasis parameters, which are traditionally controlled in clinical practice.

Dynamics of the amplitude of the circadian rhythm GPVR, in $\text{dyn}\cdot\text{cm}^{-5}$.

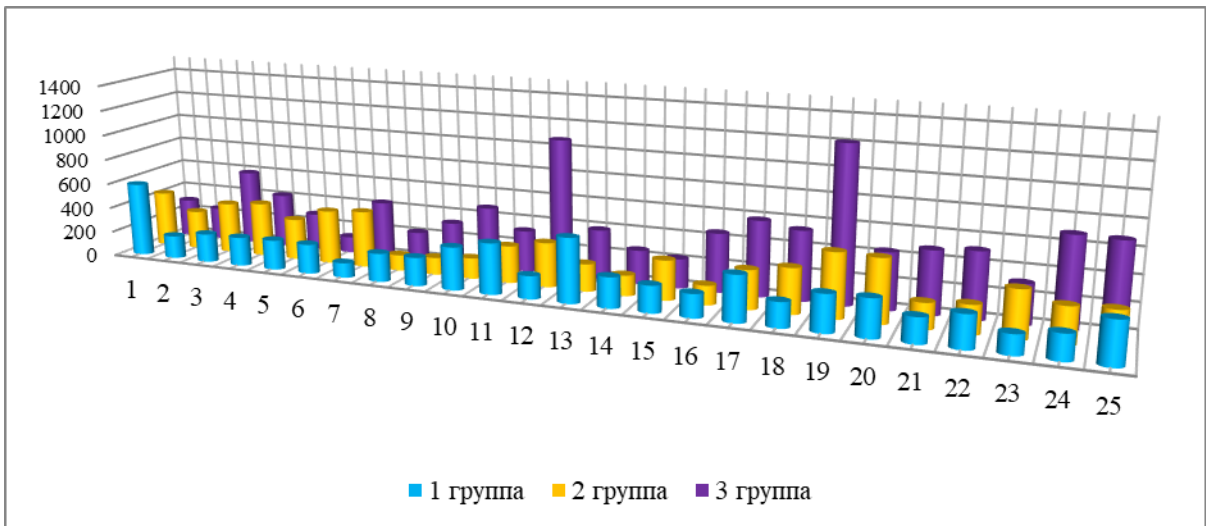


Fig.4

Changes in the amplitude of diurnal fluctuations occurred in a wave-like manner, predominantly following weekly rhythms. So, in group 1, 7, 5, 4, 4, 5 day waves were quite distinguishable. In group 2 there are 4, 5, 6, 5, 5 daily fluctuations. In group 3 there are 6,4,6,6,4 daily fluctuations. Moreover, the greatest amplitude of daily changes in GPVR was observed in group 3 at 12.19 days. Obviously, it is difficult to comply with the main condition for the effectiveness of vasoactive correction - this is the maintenance of a stable tone of peripheral vessels adequate to the consistently increased needs of the brain and other tissues in oxygen.

Table 2

The severity and duration of GPVR acrophase shifts

	norm	moderate shift	inversion
Group 1	12%	40%	48%
Group 2	28%	40%	32%
Group 3	0	56%	44%

As shown in tab. 2, the normal acrophase position prevailed in group 2, occupying 28% of the duration of intensive therapy and was absent in group 3. At the same time, the longest inversion of the GPVR circadian rhythm continued in group 1 (48%), which indicated a significant and longest stress change in the structure of daily biorhythms of GPVR, caused mainly by peripheral vascular spasm in group 1 of a compensatory nature during adaptation in the acute period of CSTBI.

Correlation of GPVR with hemodynamic parameters in the acute period of CSTBI.

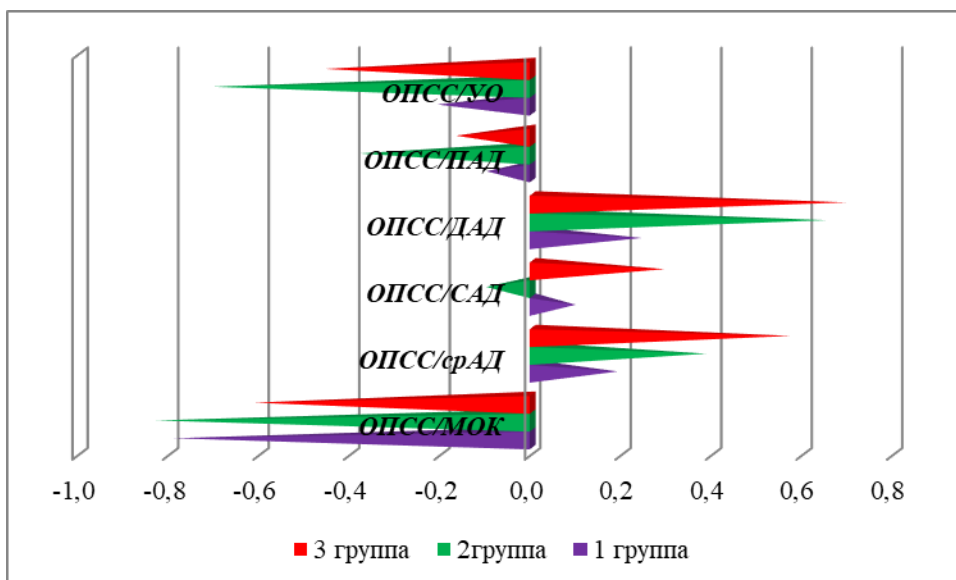


Fig.5

A reliably negative correlation between GPVR and IOC (-0.8) was found in group 1, in group 2 - (-0.8) and less pronounced in group 3 - (-0.6), as well as a negative correlation between the GPVR indicator and VO in 0, 2 group (-0.7) was characterized by a tendency towards the formation of a hyperdynamic type of hemodynamics in all the injured. While a positive correlation was noted between GPVR and DBP in 3 - (0.7) and in group 2 - (0.6). The latter makes it possible, by the mesor of the circadian rhythm DBP, to be guided by the state of general peripheral resistance in persons over 41 years old in the acute period of CSTBI. An attempt to identify the features of adaptive changes in the GPVR circadian rhythm depending on the time elapsed from the moment of injury revealed the following.

Table 3.

Correlation links GPVR by group

	from 1 to 8 days			from 9 to 17 days			from 18 to 25 days		
	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
GPVR/CO	-0.8	-0.9	-0.7	-0.8	-0.9	-0.5	-1.0	-0.9	-0.6
GPVR/avBP	-0.1	0.4	0.4	0.1	0.1	0.7	-0.2	0.6	0.6
GPVR/SBP	0.0	0.2	0.0	0.0	-0.5	0.4	-0.7	-0.5	0.4
GPVR/DBP	0.0	0.8	0.6	0.2	0.4	0.8	0.3	0.8	0.7
GPVR/PBP	-0.3	0.1	-0.7	-0.4	-0.8	0.0	-0.8	-0.5	0.0
GPVR/SV	-0.3	-0.3	-0.8	-0.3	-0.7	-0.2	-0.9	-0.9	-0.5

A strong negative correlation between GPVR and CO was weakened only in patients of group 3 from 9 to 17 days (-0.5), and from 18 to 25 (-0.6). An inverse strong dependence of SV on GPVR in the first week was revealed only in group 3 (-0.8), from 9 to 17 days (-0.7) in group 2, in the third week of intensive therapy in patients of groups 1 and 2 (-0.9, respectively). A reliably significant direct correlation between DBP and GPVR indicators appeared in group 2 (0.8) in the

first week of treatment, in group 3 in the second week (0.8), and in patients older than 41 years from 18 to 25 days, amounting to 0, 8 and 0.7. Direct dependence of avBP on GPVR was found only in group 3 on days 9-17 (0.7). A strong inverse effect of GPVR on PBP was observed from 1 to 8 days in group 3 (-0.7), from 9 to 17 days in group 2 (-0.8), from 18 to 25 days only in group 1 (-0.8).

Thus, in the most complex adaptation process at different times after injury, different compensatory mechanisms are included, early correlations weaken or disappear, new correlations appear and strengthen. But for 25 days after the injury, despite the increased mesor of the circadian rhythm GPVR and the normal values of the mesor of the circadian rhythm CO, the tendency to the hypercirculatory type of blood circulation persists in all age groups. Apparently, the effectiveness of treatment is in this situation depending on the maintenance of the functional activity of organs, the required level of cellular metabolism with the appropriate delivery of oxygen and the constituents of metabolically active substances necessary in the fight against the energy deficit state, which is inevitable under conditions of severe traumatic stress with concomitant STBI.

Conclusion. In the first 25 days, the GPVR circadian rhythm mesor was increased in all groups of patients with CSTBI. The GPVR circadian rhythm consisted mainly of ultradian 3-4 hour oscillations in all patients. From 9 to 17 days, the GPVR indicators in the circadian rhythm in group 3 were higher than in the first and second groups by 13%. In the 1st group on the second week of the study there was an inversion of the circadian rhythm GPVR, in the 2nd group at 14:00, and in the 3rd group at 13:00. In group 1, 7, 5, 4, 4, 5 daytime waves of changes in the amplitude of the GPVR circadian rhythm were quite distinguishable. In group 2 there are 4, 5, 6, 5, 5 daily fluctuations. In group 3 there are 6,4,6,6,4 daily fluctuations. For 25 days after the injury, the tendency to the hypercirculatory type of blood circulation persisted in all age groups.

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