

**CIRCADIAN RHYTHM OF VEGETATIVE TONE OF
HEMODYNAMIC REGULATION IN THE PHASE OF ANURIA OF
ACUTE RENAL FAILURE IN INFANTS**

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Abstract. The data of hourly monitoring by the method of assessing autonomic tone (AUT) in 37 children with acute renal failure (ARF) who were admitted with anuria from 1 to 5 days at the age of 10 months to 3 years 4 months were studied. A moderate tendency to increase the mesor of the circadian rhythm of AUT was revealed in groups 1 and 3, and a normal value in children of group 2 on the first day of intensive therapy for the anuric phase of acute renal failure. In the dynamics, there was a moderate tendency to increase sympathotonic activity by 10-20% in patients of groups 1 and 2, in group 3 the increase in sympathotonic influences was 30-40%. An unfavorable factor that creates an increased risk of aggravating the severity of the condition is a significantly significant excess of OBT in group 3 at night (from 11 pm to 5 am by 30%). A greater inclination to the hyperdynamic nature of changes in the circulatory system was found in group 2, in group 1, and a trend in group 3. The formation of the hyperdynamic type of hemodynamics was accompanied by an increase in myocardial oxygen demand.

Keywords: circadian rhythm, autonomic tone, acute renal failure, infants.

Relevance. Causes of renal acute renal failure in children include diseases of the renal parenchyma (glomerulonephritis, autoimmune and vascular damage to the kidney tissue), exposure to drugs (antibiotics and others), and nephrotoxins. Serious consequences of oliguria/anuria are pulmonary and cerebral edema, hypervolemia (volume overload), hyperkalemia, acidosis, drug toxicity. The goal of

intensive therapy for acute renal failure is the prevention of these potentially fatal complications and renal ischemia: hemodynamic optimization, active treatment of hypoxia, provision of zero or even negative balance for the prevention of pulmonary edema in anuria, monitoring of blood electrolyte composition, acid-base balance (ABB). One of the leading pathogenetic mechanisms for the development of acute renal failure is a hypersympathotonic reaction that causes spasm of peripheral, including renal vessels, ensuring the adequacy of compensatory centralization of blood circulation in conditions of dehydration (hypovolemia), other stress reactions of the body to external, internal extreme influences. A feature of the VNS function in infancy is hyperreactivity and rapid depletion of resources under conditions accompanied by compensatory mobilization of the VNS function. However, there is not enough information in the literature on monitoring the state of the autonomic balance in the anuric phase in children under 3 years of age with acute renal failure, which served as the basis for this study [1-6].

Goal of the work. To study the features of the circadian rhythm of OBT in children with acute renal failure in the period of anuria at an early age.

Material and research methods. The data of hourly monitoring by the method of assessing vegetative tone (AVT) in 37 children with ARF admitted to the ICU of RRCEMMP with anuria from 1 to 5 days at the age of 10 months to 3 years 4 months from the ICU of regional children's hospitals and branches of RSC EMC were studied. Prior to admission to the clinic, all patients received anti-inflammatory therapy aimed at the treatment of ARI-2, pneumonia 25, glomerulonephritis - 8, AII-3 patients. According to the indications, due to severe progressive respiratory failure, patients were provided with invasive mechanical respiratory support from the first day. All patients underwent hemodialysis, 4 patients underwent hemodialysis in combination with plasmapheresis under the control of hemodynamics, acid-base status (ABS), respiratory system, supportive, antibacterial, anti-inflammatory, syndromic corrective intensive therapy according to the recommendations in the literature. A favorable outcome with the restoration of full functional activity of the kidneys and discharge from the hospital was observed in 27 children (groups 1 and 2), an unfavorable outcome in 10 children (group 3). The first group consisted of patients who received intensive care in the ICU for up to 10 days (12), the second - children (17) with a favorable outcome after intensive care for 11-65 days.

As shown in Table 1, the duration of intensive care in children of groups 2 and 3 significantly exceeded the duration of treatment in the ICU in group 1 by 20 or more days ($p < 0.05$, respectively). In group 2, the duration of mechanical respiratory support (MRS) was 18.6 ± 8 days, in group 3, a longer MRS, unfortunately, did not improve the outcome of the disease.

Table 1.
Characteristics of patients

Groups	Age, month	Start of IVL, days	Duration of MRS, days	In ICU, days
1	29±2,8	0	0	7,8±1,5
2	19±7,7	4,3±3,5	18,6±7,6	27,8±4,3*
3	30,5±6,5	5,5±0,5	25,5±6,7	30,7±6,8*

* - the difference is significant relative to the indicator in group 1.

Results and its discussion.

Table 2
Dynamics of mesor circus rhythm AVT

Days	1 group	2 group	3 group
	1,2±0,1	1,0±0,1	1,1±0,1
	1,2±0,1	1,3±0,02	1,3±0,1
	1,1±0,02	1,2±0,1	1,3±0,1
	1,2±0,1	1,2±0,01	1,4±0,1*
	1,0±0,01	1,3±0,1	1,4±0,1**
	1,1±0,1	1,2±0,01	1,5±0,1* **
	1,2±0,1	1,1±0,1	1,5±0,1* **
	1,2±0,1	1,2±0,1	1,5±0,1* **
	1,1±0,1	1,2±0,1	1,5±0,1* **
	1,2±0,1	1,2±0,1	1,4±0,1*
		1,3±0,1	1,4±0,1*
		1,3±0,1	1,4±0,1*
		1,3±0,1	1,4±0,1*
		1,2±0,1	1,4±0,1*
		1,2±0,1	1,3±0,1
		1,3±0,1	1,4±0,1
		1,2±0,1	1,4±0,1
		1,2±0,0	1,5±0,1
		1,2±0,1	1,4±0,1
		1,3±0,1	1,5±0,1
		1,2±0,1	1,4±0,1
		1,3±0,1	1,3±0,1
		1,2±0,1	1,4±0,1
		1,3±0,1	1,5±0,2
		1,4±0,1	1,5±0,1
		1,3±0,1	1,3±0,1

		1,2±0,1	1,3±0,1
		1,2±0,1	1,5±0,1
		1,3±0,2	1,4±0,1
		1,5±0,2	1,4±0,1

Table 3

Average values of AVT in the circadian rhythm

Hours	1 group	2 group	3 group
8	1,2±0,1	1,2±0,1	1,4±0,1
9	1,2±0,1	1,2±0,1	1,4±0,1
10	1,2±0,1	1,2±0,1	1,4±0,1
11	1,2±0,1	1,3±0,1	1,4±0,1
12	1,2±0,1	1,2±0,1	1,4±0,1
13	1,2±0,1	1,2±0,1	1,4±0,1
14	1,1±0,1	1,3±0,1	1,4±0,1 ^m
15	1,2±0,1	1,3±0,1	1,4±0,1
16	1,1±0,1	1,3±0,1	1,4±0,1 ^m
17	1,2±0,1	1,2±0,1	1,4±0,2
18	1,2±0,1	1,3±0,1	1,4±0,1
19	1,2±0,1	1,3±0,1	1,4±0,1
20	1,2±0,1	1,2±0,1	1,4±0,1
21	1,2±0,1	1,2±0,1	1,4±0,1
22	1,2±0,2	1,3±0,1	1,4±0,1
23	1,1±0,1	1,3±0,1	1,4±0,1 ^m
24	1,1±0,1	1,2±0,1	1,4±0,1 ^m
1	1,1±0,1	1,2±0,1	1,4±0,1 ^m
2	1,1±0,1	1,2±0,1	1,4±0,1 ^m
3	1,2±0,1	1,3±0,1	1,4±0,1
4	1,1±0,1	1,2±0,1	1,4±0,1 ^m
5	1,1±0,1	1,3±0,1	1,4±0,1 ^m
6	1,2±0,1	1,3±0,1	1,4±0,1
7	1,2±0,1	1,2±0,1	1,4±0,1

*-certainly relatively indicator in 1 day.

^m- significant relative to group 1

A moderate tendency to increase the mesor of the circadian rhythm of AVT was revealed in groups 1 and 3 and a normal value in children of group 2 on the first day of intensive therapy for the anuric phase of acute renal failure. In dynamics, there was a tendency to increase sympathotonic activity by 10-20% in patients

of groups 1 and 2 (Table 2), while in the most severe group on days 4-14 and in the next 16-30 days there was a significant increase in sympathotonic effects by 30–40% (p<0.05, respectively), despite the ongoing complex anti-inflammatory, vasodilating, stress-limiting therapy with mechanical respiratory support from the first day of observation due to the more severe course of acute pneumonia, secondary encephalopathy, myocarditis with progressive decompensation of functions, development of multiple organ failure. In Fig. 1, attention is drawn to the correspondence of the severity of the hypersympathotonic reaction to the severity of the condition of the patients. Moreover, in the process of adaptation of the autonomic regulation of hemodynamics, changes in the mesor of the circadian rhythm were of a wave-like nature with a period of fluctuations in the 1st group of 8 days, in the 2nd - 7.7.5.6.5 days, in the 3rd - 15.7.5.5 days with the most pronounced deformation of the waves characterizing the instability of autonomic regulation, due to more pronounced intoxication, a violation of the water-electrolyte, acid-base balance in the most severe patients.

A significantly significant difference in the mesor of the circadian rhythm of AVT in group 3 relative to the index on days 5-9 of patients in group 1 by 30-40% was revealed, which confirms a more pronounced sympathotonic reaction that accompanies the systemic inflammatory response of the body in children with an unfavorable outcome. From this it follows that the ongoing intensive anti-inflammatory therapy was significantly less effective than in the 1st group of children. The latter is possibly an indicator of a more virulent infection, an indicator of the stage of irreversible disorders at the cellular, tissue, organ level due to aggravation of the general condition due to the addition of homeostasis deviations to the primary inflammatory process with predominant damage to the functional system of the kidney parenchyma. The latter was manifested by the most pronounced hypersympathotonic reaction to ongoing ischemia during treatment, damage to the glomerular apparatus of the kidneys. This is confirmed by a higher level of sympathetic activity regardless of the time of day in group 3 (Fig. 2). An unfavorable factor that creates an increased risk of aggravation of the severity of the condition, ineffectiveness of medical correction of deviations is a significantly significant excess of OBT in group 3 relative to the indicator of children in group 1 at night (from 11 p.m. to 5 a.m. by 30%). Taking into account the identified feature of autonomic restructuring in acute renal failure, it seems to make sense to revise the drug correction with an emphasis on the expediency of strengthening the effect on the correction of perfusion deviations at night (Table 3).

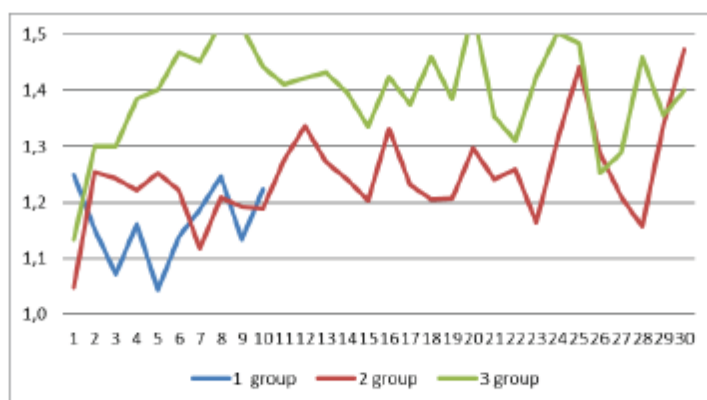


Figure 1. Dynamics of the mesor circus of the AVT rhythm in acute renal failure up to 3 years

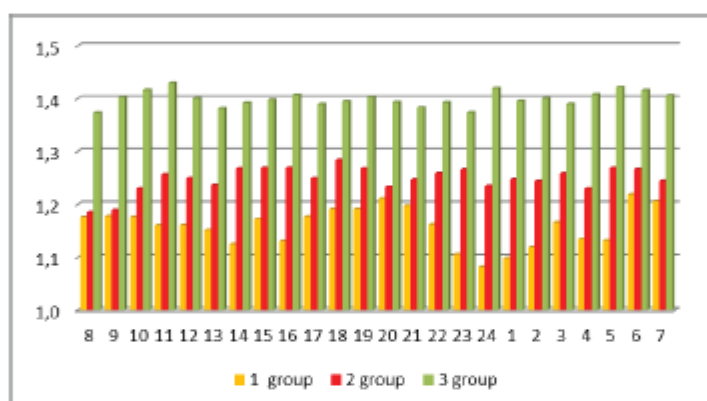


Figure 2. Average level of AVT in the circadian rhythm

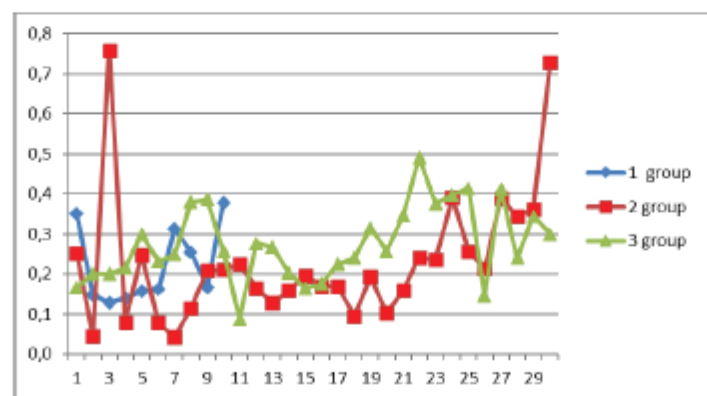


Figure 3. Dynamics of the amplitude of the circadian rhythm of AVT up to 3 years

The most pronounced amplitude of the daily fluctuations in AVT on days 3 and 30 in the 2nd group of children drew attention, which, apparently, was adaptive in nature on day 3 at the peak of the inflammatory response, a repeated increase in the amplitude of the OBT circadian rhythm on day 30 was due to a decrease in stress-limiting, sedative therapy in the process of restoring spontaneous breathing, extubation (Fig. 3).

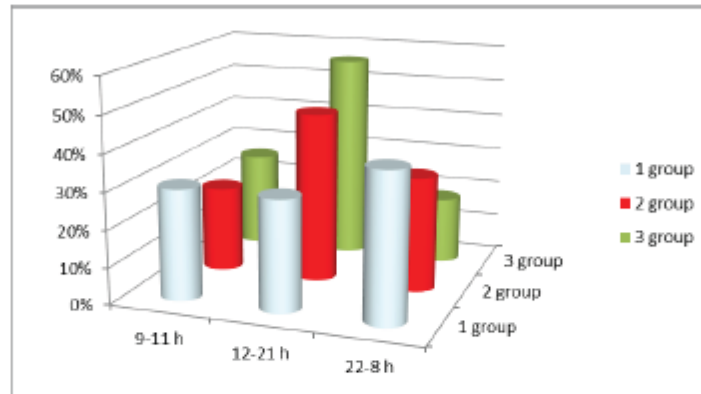


Figure 4. The duration of the inversion of the circadian rhythm according to the severity of the condition of patients with acute renal failure in the phase of anuria under the age of 3 years

As shown in fig. 4, in percentage terms, the longest inversion of the AVT circadian rhythm was in group 1. But, if we take into account the duration of intensive care in the ICU, it turned out that the longest was the inversion of the circadian rhythm in children with acute renal failure in group 2, amounting to 9, in group 3 - 5, and in group 1 - 4 days. It can be assumed that the circadian rhythm of the sympathetic nervous system is also involved in the process of adaptation to new conditions of existence in conditions of an inflammatory reaction in acute renal failure, which, depending on the severity of kidney damage, was more actively manifested with the preservation of reserve capabilities, a lesser degree of CNS damage in group 1. A decrease in the severity of the adaptive restructuring of the AVT circadian rhythm in the 2nd group of children was a manifestation of not only a more active corrective, drug, stress-limiting effect due to a greater degree of damage to the function of the kidneys and other organs (pneumonia, secondary encephalopathy), but also the inadequacy of compensatory reactions of organs due to with the depletion of energy resources. And the most pronounced damage to the kidneys, as well as the regulatory function of the autonomic nervous system in group 3, led to an even more significant decrease in the adaptive capacity due to a change in the compensatory reaction of the functional activity of the VNS, which played a certain role in the outcome of this severe pathological condition.

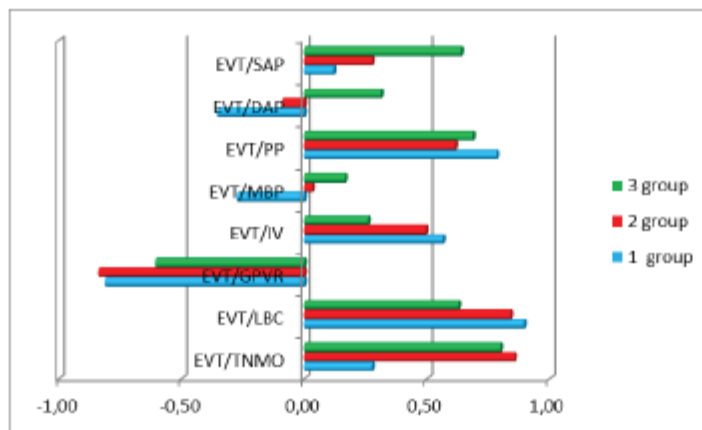


Figure 5. Correlations of AVT in ARF under the age of 3 years

The most pronounced stimulating effect of sympathetic activity on the IOC was found in group 1 (0.89), in group 2 (0.84) and in group 3 (0.63). An inversely directed correlation between the dynamics of the mesor of the circadian rhythm of the OBT and OPSS, which amounted to (-0.81) in group 1, (-0.84) in group 2, and (-0.61) in group 3, testified to a significantly greater inclination to the hyperdynamic nature of changes circulatory system in group 2, in group 1, and a trend in group 3. The formation of the hyperdynamic type of hemodynamics was accompanied by an increase in myocardial oxygen demand. The latter turned out to be the most significant in group 2 (0.86), in group 3 (0.8), and in group 1 (0.28) (Fig. 5). That is, the more severe the anuria phase was in infants, the more unfavorable the state of myocardial trophism was due to the progression of oxygen deficiency in terms of the severity of the condition and the severity of impaired function of the kidneys and other systems of the child's body up to 3 years.

Conclusion. A moderate tendency to increase the mesor of the circadian rhythm of OBT was revealed in groups 1 and 3, and a normal value in children of group 2 on the first day of intensive therapy for the anuric phase of acute renal failure. In the dynamics, there was a moderate tendency to increase sympathotonic activity by 10-20% in patients of groups 1 and 2, in group 3 the increase in sympathotonic influences was 30-40%. An unfavorable factor that creates an increased risk of aggravating the severity of the condition is a significantly significant excess of OBT in group 3 at night (from 11 pm to 5 am by 30%). A greater inclination to the hyperdynamic nature of changes in the circulatory system was found in group 2, in group 1, and a trend in group 3. The formation of the hyperdynamic type of hemodynamics was accompanied by an increase in myocardial oxygen demand.

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