https://doi.org/10.15360/1813-9779-2022-6-22-29

The Early Use of Selective Hemoadsorption Based on a Hyper-Crosslinked Styrene-Divinylbenzene Copolymer in Patients with Toxic Rhabdomyolysis Complicated by Acute Kidney Injury (Multicenter Randomized Clinical Trial)

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For citation: *Sergey V. Masolitin, Denis N. Protsenko, Igor N. Tyurin, Marat A. Magomedov, Timur G. Kim, Lyudmila A. Grishina, Andrey O. Bykov, Elizaveta B. Gelfand, Olga V. Ignatenko*. The Early Use of Selective Hemoadsorption Based on a Hyper-Crosslinked Styrene-Divinylbenzene Copolymer in Patients with Toxic Rhabdomyolysis Complicated by Acute Kidney Injury. *Obshchaya Reanimatologiya = General Reanimatology*. 2022; 18 (6): 22–29. https://doi.org/10.15360/1813-9779-2022-6-22-29 [In Russ. and Engl.]

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Summary

Rhabdomyolysis (RM) is a clinical and laboratory syndrome with the underlying destruction of myocytes and the release of intracellular debris into the systemic circulation. In more than 55% of cases, RM is complicated by acute kidney injury (AKI), which necessitates various methods of extracorporeal detoxification and currently is a controversial issue.

Aim: to improve the results of treatment of patients with RM of toxic origin complicated by AKI by using early selective hemoadsorption (SH).

Material and methods. The study included 36 patients divided into 2 groups. Group 1 included 24 patients who received standard therapy and hemodiafiltration (HDF) as a life-saving intervention. Group 2 comprised 12 patients who underwent early SH to prevent the progression of AKI. We performed a comparative analysis of clinical and laboratory parameters and treatment outcomes in the groups.

Results. The use of SH was associated with reduced level of myoglobin on day5 of therapy from 384.1 to 112.4 μg/l (70.7%) vs 335.15 to 219.1 μg/l (34.6%) reduction in the conservative therapy group. By day 7, this parameter was 18.8 (95.1%) and 142.4 (57.5%), respectively (P=0.012). The level of cystatin-C decreased on day 5 from 17.3 to 3.2 mg/l (81.5%) in group 2 and from 14.9 to 11.7 mg/l (21.5%) in group 1. By day 7, this parameter decreased to 2.5 (85.6%) and 14.1 (5.3%) mg/l, respectively (P=0.001). The length of ICU stay in group 2 was 7 (6; 9) days, while in the conservative therapy group it was 12 (7; 13) days (P=0.04). The hospital stay was 12 (10; 16) and 22 (14,5; 24,5) days, respectively (P=0.028).

Conclusion. The early use of SH in the intensive therapy helped decrease the levels of markers of endogenous intoxication, AKI severity, improve the filtration capacity of the kidneys, and reduced the length of stay in the ICU and hospital.

Keywords: rhabdomyolysis; hemoperfusion; myoglobin; cystatin-C; hemodiafiltration; acute kidney injury

Conflict of interest. The authors declare no conflict of interest.

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Introduction

Rhabdomyolysis (RM) is a clinical and laboratory syndrome with the underlying damage of the transverse striated muscles (myocytes) of different etiology, involving release of intracellular contents into the bloodstream [1, 2].

As a result of myocyte damage and destruction, such numerous intracellular substances as myoglobin, CPK (creatine phosphokinase), lysosomal and mitochondrial enzymes, histamine, serotonin, cellular wall components, oligo-, polypeptides, etc. enter the bloodstream. The resulting systemic toxemia associates with multiple organ failure syndrome [3]. The most frequent and widespread complication in RM is acute kidney injury (AKI) syndrome, which is associated with severe disease and adverse clinical outcome [4, 5]. Myoglobin plays a fundamental role in the development and progression of AKI [6, 7].

Currently, the main concept of extracorporeal detoxification (ECD) involves removal of myoglobin and other factors of endogenous intoxication from the bloodstream [8, 9]. Various techniques and regi-

mens of renal replacement therapy (RRT) have different efficacy in reducing the myoglobin content in blood [4, 10–13]. However, the early use of various ECD techniques to prevent the development and progression of AKI currently has no enough evidence and cannot be recommended for general use [5, 6, 14].

Novel devices for selective hemoadsorption could be potentially effective in the treatment of AKI, as they can eliminate a certain range of endogenous toxic substances from the systemic bloodstream including myoglobin and other molecules. However, these sorption systems have been only occasionally employed and have been described in a limited number of studies [15–18].

Development and application of new sorption systems capable to selectively eliminate specific range of substances from the systemic circulation prompts further study of their possible effective single or combined use in treatment of RM complicated with AKI [19–21].

The aim of the study: to improve the results of treatment of patients with toxic RM complicated by AKI by using early selective hemoadsorption (SHA).

Material and Methods

A prospective multicenter randomized study included 36 patients aged 20 to 41 years who were treated in the intensive care unit of N. I. Pirogov City Clinical Hospital No. 1 and S. S. Yudin City Clinical Hospital from 2017 to 2020 with a diagnosis of toxic rhabdomyolysis complicated by AKI. Patients were randomized using the envelope method. The study was conducted in accordance with the Declaration of Helsinki after obtaining permission from the local ethical committee of the Pirogov City Clinical Hospital dated January 13, 2017. Criteria for inclusion of patients in the study were history or clinical and/or laboratory data indicating acute poisoning; rhabdomyolysis (CPK level 1000 Units/L); clinical and laboratory signs of AKI. Exclusion criteria were age less than 18 years, pregnancy, chronic muscle diseases (muscular dystrophy, inflammatory myopathy, etc.), injuries of any localization; surgical treatment; absolute contraindications for ECD methods such as ongoing bleeding, terminal state.

All RM patients included in the study had clinical and laboratory signs of persistent AKI despite the standard intensive therapy during 12–24 hours from the moment of admission to ICU. Standard intensive therapy administered to all patients upon admission included fluid therapy for acid-base and water-electrolyte balance correction; diuretic therapy; prevention of thromboembolic complications and gastrointestinal stress ulcers; nutritional support as well as, if indicated, respiratory and inotropic/vasopressor support.

At the time of inclusion in the study, the clinical groups were completely comparable and were not significantly different from each other ($P>0.05$ for all parameters, Table 1).

All patients underwent standard monitoring of hemodynamic parameters (blood pressure, heart rate, respiratory rate) and clinical and laboratory parameters (clinical blood count with leukocyte morphology, biochemical analysis, coagulation test, urinalysis, acid-base balance) during intensive therapy. Statistical analysis included the worst values of parameters registered during the day. The levels of CPK and myoglobin were assessed to evaluate endogenous intoxication and RM severity. The severity of organ dysfunction was assessed daily using SOFA scale, and the risk of adverse outcome was assessed using APACHE II scale. Diagnosis of AKI in all patients was made based on KDIGO (Kidney Disease: Improving Global Outcomes) guidelines, on admission and daily thereafter. To assess AKI markers, plasma cystatin-C level was determined, and to assess the changes in renal function, urine output rate was assessed and GFR was calculated using endogenous creatinine clearance in the blood and urine (Rehberg-Tareyev's test). Statistical analysis was performed based on the worst values of parameters during a day.

During the study, patients were randomized into two clinical groups.

Group 1 included 24 patients, whose standard intensive care during the first 24 hours in ICU did not reduce the AKI severity. During the treatment of the group 1 patients, the standard indications for the initiation of RRT were followed, i. e., life-threatening severe renal dysfunction despite the basic full-fledged intensive care therapy. These indications included severe uremia with increased blood urea level over 40 mmol/l; anuria or oliguria resistant to diuretics; increased blood potassium level over 6.5 mmol/l; severe metabolic acidosis with pH less than 7.15 resistant to fluid therapy. The above indications for urgent initiation of RRT were identified during treatment in 21 patients (87.5%) from group 1. Renal replacement therapy was performed in the HDF (hemodiafiltration) mode.

Group 2 included 12 patients with toxic RM complicated by AKI, whose basic intensive care during the first day after admission to ICU did not result in reduced severity of AKI. When no effect of basic intensive therapy was seen within 12–24 hours after admission to ICU in patients of this group, selective hemoadsorption was used for active detoxication and nephroprotection in early stages of AKI (KDIGO 1 or 2). If severe life-threatening renal failure developed, the RRT in HDF mode was initiated. In this group, indications for urgent RRT initiation were found in 9 patients (75%) during the treatment.

The post-dilution HDF using a 5008S machine (Fresenius Medical Care, Germany) was performed. High-permeability FX800HDF or FX1000HDF he-

Table 1. Baseline values of clinical and main laboratory parameters in the study groups, *Me* (*Q1*; *Q3*).

Parameter	Parameters values in groups		*P*-value
	Group 1, *n*=24	Group 2, *n*=12	
Clinical parameters			
Males, *n*	17	9	1.0
Females, *n*	7	3	
Age, years	34 (27; 36)	35 (20; 41)	0.74
Weight, kg	86 (73; 98)	92 (84; 103)	0.83
SOFA, points	5 (5; 7)	6 (5; 8)	0.92
APACHE II, points	17 (17; 20)	18 (15; 21)	0.58
KDIGO, stage	0–I	0–I	1.0
MAP, mmHg	68 (52; 74)	62 (50.1; 70.2)	0.38
Heart rate, beats per minute	107 (102; 114)	111 (99; 121)	0.81
GFR, ml/min/1.73 m^2	84 (50.5; 87)	75 (55; 80)	0.28
PaO_2/FiO_2, mm Hg	291 (282; 308)	287 (270; 312)	0.41
CVP, cm H_2O	0 (0; 1)	1 (0; 1)	0.56
Urine output, ml per hour	43 (37; 61)	40 (32; 54)	0.29
Laboratory parameters			
Red blood cells, $\times10^{12}$/l	4.64 (4.46; 5.28)	5.13 (4.7; 5.88)	0.17
Hemoglobin, g/l	162 (159; 165)	163 (153; 177)	0.78
Hematocrit, %	42.9 (40.3; 46.7)	51.3 (48.9; 55.9)	0.26
Platelets, $\times10^9$/l	221 (196; 243)	210 (196; 232)	0.83
White blood cells, $\times10^9$/l	9.2 (6.8; 11.7)	11.1 (7.2; 13.7)	0.38
pH	7.1 (7.08; 7.3)	7.12 (6.9; 7.2)	0.31
BE, mmol/l	–4.2 (–5.5; –3.15)	–5.3 (–6.3; –3.6)	0.26
Potassium, mmol/l	3.8 (3.4; 4.2)	3.7 (3.2; 4.6)	0.42
Sodium, mmol/l	138 (132; 144)	133 (129; 142)	0.67
Calcium, mmol/l	0.58 (0.44; 0.82)	0.6 (0.51; 0.77)	0.29
Chloride, mmol/l	106 (95.1; 109)	104 (92.3; 107.7)	0.81
Lactate, mmol/l	6.2 (4.6; 8.1)	5.9 (5.1; 7.3)	0.32
Total protein, g/l	69 (61.1; 73.8)	67.7 (61.2; 78.3)	0.41
Albumin, g/l	33.2 (30.3; 35.5)	34.1 (31.2; 41.4)	0.54
Urea, mmol/l	11.1 (7.45; 14.25)	12.5 (10.6; 13.7)	0.83
Creatinine, µmol/l	148.2 (124.5; 181.8)	182.6 (135.6; 197.5)	0.21
ALT, U/l	64 (47.5; 107.5)	106 (68.4; 487.6)	0.31
AST, U/l	160.1 (133.1; 213.1)	202.1 (180.2; 281.2)	0.44
Total bilirubin, µmol/l	11.9 (8.2; 15.4)	15.1 (8.3; 20.6)	0.72
Alkaline phosphatase, mmol/l	98 (72; 123)	128 (98.1; 145)	0.51
LDH, IU/l	245.1 (130.3; 348.15)	315.5 (101.5; 693.85)	0.92
CPK, U/l	10745 (6726.3; 14192)	9288 (8124; 17282)	0.76
CRP, mg/l	89 (45.7; 99.5)	74 (50.8; 88.3)	0.69
PCT, ng/ml	4.1 (2.61; 6.2)	3.86 (3.47; 5.3)	0.61
Myoglobin, µg/l	335.15 (266; 413.7)	384.1 (296.5; 428.8)	0.74
Cystatin C, mg/l	14.9 (12.5; 18.5)	17.3 (14; 18.95)	0.86
APTT, s	26.6 (23; 27.5)	25.5 (23.9; 25.6)	0.14
INR	1.08 (1.02; 1.13)	1.06 (0.9; 1.1)	0.49
Fibrinogen, g/l	4.4 (3.4; 4.9)	4.3 (3.7; 5.3)	0.95

Note. Differences between groups (*P*-values) were assessed using the Mann–Whitney *U*-test, for quantitative (binary) variables, Fisher's exact test was used. MAP — mean arterial pressure; GFR — glomerular filtration rate; CVP — central venous pressure; PaO_2/FiO_2 — ratio of the partial pressure of oxygen in the arterial blood to the fraction of oxygen in the inhaled gas; ALT — alanine aminotransferase; AST — aspartate aminotransferase; LDH — lactate dehydrogenase; CPK — creatine phosphokinase; CRP — C-reactive protein; PCT — procalcitonin; APTT — activated partial thromboplastin time; INR — international normalized ratio.

mofilters (B.Braun Avitum AG, Germany) were used as a mass-exchange device. During hemodiafiltration the following parameters were used: blood flow rate, 250–300 ml/min, dialysate flow rate, 500–600 ml/min; ultrafiltration rate per hour depended on the severity of overhydration and ranged from 100 to 1000 ml/h. The RRT was performed for 4–6 hours daily or every other day until renal function was restored.

The SHA was performed using the MultiFiltrate apparatus (Fresenius Medical Care, Germany) in hemoperfusion mode with the Efferon CT adsorption system (Russia), using a standard «multiFiltrate Cassette» cartridge (Fresenius Medical Care, Germany). The SHA was carried out at the blood flow rate of 100–150 ml/min. The duration of the session was 6 to 8 hours. Anticoagulation was achieved using continuous infusion of unfractionated heparin

Table 2. Changes in the studied parameters from days 1 to 7 of treatment, *Me* (*Q1*; *Q3*).

Group	Values			
	Day 1	Day 3	Day 5	Day 7
Myoglobin, μg/l				
1, *n*=24	335.15 (266; 413.7)	318.25 (215.2; 355.8)	219.1 (168.4; 268.7)	142.4 (129.3; 158.4)
2, *n*=12	384.1 (296.5; 428.8)	236.1 (187.3; 253.3)	112.4 (94.9; 122.45)	18.8 (15.4; 19.4)
P-value		0.28	0.003	0.012
CPK, IU/l				
1, *n*=24	10745 (6726; 14192)	2549 (2036; 5606)	1356 (1104; 3355)	789 (619; 1119)
2, *n*=12	9288 (8002; 17282)	1424 (1241; 2941)	520 (256; 702)	101 (99; 146)
P-value		0.24	0.02	0.002
Cystatin-C, mg/l				
1, *n*=24	14.9 (12.5; 18.5)	16.2 (13.2; 18.6)	11.7 (11.2; 15.4)	14.1 (9.5; 16.4)
2, *n*=12	17.3 (14; 18.9)	12.9 (11.1; 16.3)	3.2 (2.2; 5.3)	2.5 (2.2; 5.6)
P-value		0.32	0.003	0.001

Note. Differences between groups were assessed using the Mann–Whitney *U*-test.

500–1000 units/hour with coagulation parameters monitoring. To perform ECD, a double-lumen perfusion catheter was placed in a central vein.

Statistical methods. The results obtained during the study were presented as a median, 25th and 75th percentiles. The Kolmogorov–Smirnov method was used to assess the data distribution. Nonparametric Mann–Whitney and Kruskal–Wallis criteria were used to test statistical hypotheses. Groups were compared by qualitative characteristics using Fisher's exact criterion. Wilcoxon criterion was used to test the significance of differences between the changes in the values of parameters. The differences were considered significant at $P<0.05$. No adjustment for multiplicity was made. The statistical analysis of results was performed using Microsoft Excel with Real Statistics 2021 (by Charles Zaiontz).

Results

Changes in the markers of endogenous intoxication and severity of acute kidney injury.

To determine the detoxification capability of various methods of extracorporeal detoxification, we assessed the levels of myoglobin being the major pathogenetic marker of AKI (Table 2).

Significant positive intra-group changes were observed. Myoglobin level by day 3 of life-saving HDF decreased by 5.04% from the baseline (*P*=0.012), whereas in group 2 (selective hemoadsorption) a decrease of 38.5% from baseline values was observed (*P*=0.021). By day 5 of intensive therapy the decrease was 34.6% (*P*=0.002) in group 1 and 70.7% in group 2 (*P*=0.016). By day 7, it became for groups 1 and 2 57.5% (*P*=0.002) and 95.1% (*P*=0.036), respectively. Significant intergroup differences were observed on day 5 (*P*=0.003) and day 7 (*P*=0.012) of therapy. Thus, a variable decrease in myoglobin levels was observed with different methods of extracorporeal detoxification, however, it was significantly greater with the use of SHA.

Table 2 shows the changes in CPK levels from day 1 to day 7 of intensive care therapy. Significant decrease in CPK levels was observed in both clinical groups from day 1 to day 7 of intensive care therapy (*P*=0.001). In group 1, this parameter decreased by 76.3% on day 3, by 87.4% on day 5, and by 92.6% on day 7. In Group 2, the changes were 84.7%; 94.4% and 98.9%, respectively. Notably, the changes in CPK levels in group 2 CPK were more prominent than in group 1, with the appearance of intergroup differences on days 3 and 7 of intensive therapy (*P*=0.02 and *P*=0.002, respectively, Table 2).

The changes in cystatin-C levels are considered among the most important markers of renal function which increase in the setting of acute kidney injury (Table 2).

In group 1 (life-saving HDF), insignificant changes were observed: on day 3 of therapy, we observed a 8.7% increase of cystatin-C concentration in comparison with the initial value, on day 5, 21.5% decrease, and on day 7, 5.4% reduction (*P*=0.27; 0.4; 0.16, respectively). In group 2, where SHA with further HDF was performed, the reduction in cystatin-C concentration on day 3 was 25.4%, on day 5, 81.5% and on day 7, 85.6% (*P*=0.67; 0.02; 0.003, respectively). A significant reduction in cystatin-C level in this group was observed starting from day 5 of intensive therapy. Intergroup differences were registered on the 5th and 7th days of treatment (*P*=0.003; 0.001).

Glomerular filtration rate is an important indicator of the renal functional recovery in acute kidney injury. Figure 1 shows the changes of GFR in the studied groups.

In group 2, starting from day 6 of treatment, there was a significantly higher rate of recovery of renal function than in group 1 on days 6, 7, 8, (*P*=0.04, *P*=0.01, *P*=0.03, respectively).

Assessment of the frequency and duration of RRT.

In patients with toxic rhabdomyolysis, the changes in AKI progression and the rate of life-saving RRT play a crucial role. Figure 2 shows the frequency of life-saving RRT in the groups.

In the conservative therapy group, the frequency of life-saving RRT was 85.7%, in contrast to group 2, where after prior hemoadsorption, the frequency of RRT was 66.7%. This trend in RRT between the groups, however, was not significant (P=0.38).

The results of comparative analysis showed that the duration of RRT in group 1 was 16.4 days, and in group 2, 13.7 days (P=0.047) (Fig.3).

Comparative analysis of hospitalization time and disease outcomes.

One of the most significant criteria for the effectiveness of the therapy, both therapeutic and socio-economic, is the length of stay of patients in the ICU and the hospital. Table 3 demonstrates the group differences in duration of treatment.

Table 3 shows that in group 2 patients who received hemoadsorption both parameters of treatment duration (ICU and hospital stay) were significantly less than in patients of group 1 (P=0.041 and P=0.028, respectively).

No differences in mortality between the groups were found, which can probably be explained by a small sample size.

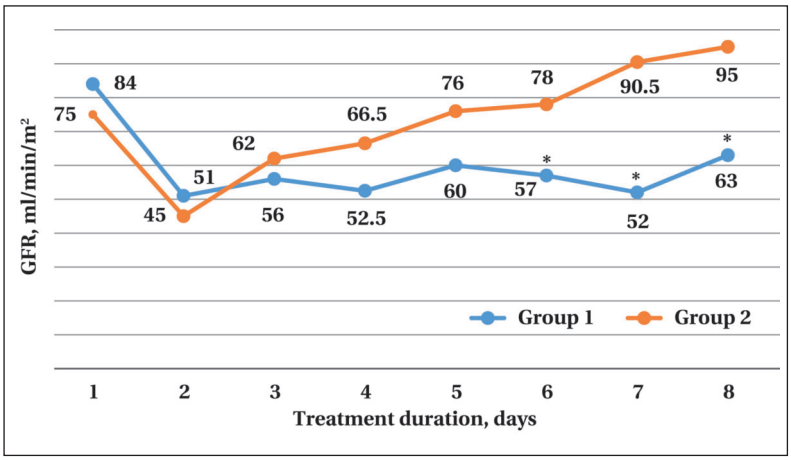

Fig. 1. Changes of GFR (Rehberg–Tareyev method) in the study groups from days 1 to 8 of intensive care.
Note. * — significant differences between groups (Mann–Whitney U-test, P<0.05).

Table 3. Duration of treatment of ICU and inpatient patients, *Me* (*Q1*; *Q3*).

Groups	Duration of treatment, days	
	ICU	Hospital
1, n=24	12 (7; 13)	22 (14.5; 24.5)
2, n=12	7 (6; 9)	12 (10; 16)
P-value	0.041	0.028

Note. Differences between the groups were assessed using the Mann–Whitney U-test, P<0.05.

Discussion

This multicenter randomized clinical trial in patients with toxic rhabdomyolysis complicated by AKI demonstrated high efficacy of early use of SHA followed by life-saving HDF compared with life-saving RRT alone. When considering the pathogenesis of rhabdomyolysis and AKI, we suggest that myoglobin level is crucial for its development being the main source and marker of systemic toxemia [8, 9, 22].

Myoglobin concentration in the SHA group decreased by 95.1% by day 7 of the therapy, in contrast to the group with life-saving RRT (57.5%) (P=0.012). Similar changes in CPK levels were obtained after using selective hemoadsorption starting from day 5 of the treatment. The high efficiency of myoglobin elimination with SHA is due to the fact that with a molecular weight of 17 kDa [23] it is removed from the bloodstream by both convection and sorption detoxification methods, while CPK molecules sized 40 to 80 kDa [24], pathognomonic for rhabdomyolysis, are removed with less efficiency [15, 16]. The elimination of endogenous intoxication factors from the systemic bloodstream manifests both in improvement of clinical and laboratory parameters and in the regression of AKI, as observed by many authors [6, 22, 25].

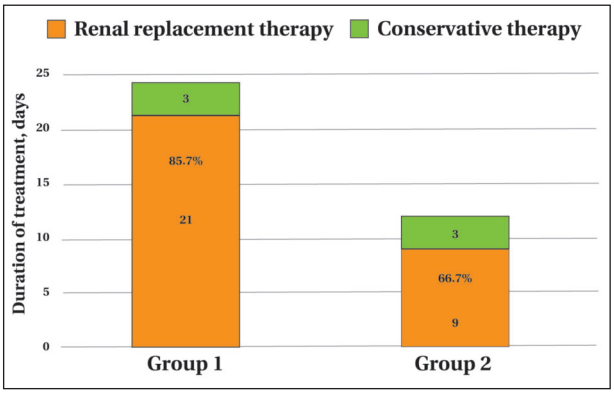

Fig. 2. Frequency of RRT in the groups.

Accelerated decrease in the levels of cystatin-C (AKI marker) after SHA is, in our opinion, directly related to the reduction of systemic toxemia factors and their nephrotoxicity, which was confirmed by other researchers [12, 22, 25, 26].

Thus, our results indicate that the earliest use of SHA results in the reduction of systemic endotoxemia and probably in an earlier recovery of renal function judging by the changes in GFR. Early use of SHA in patients with rhabdomyolysis had a positive effect on the level of endotoxemia markers, the severity of AKI, and was probably nephroprotective, which has not been yet reported in the available literature [27, 28].

Among important results of our work is a decrease in systemic toxemia expressed as reduction of myoglobin, CPK, and AKI markers, as well as an improvement in renal function and a significant decrease in the duration of RRT in SHA group, which, in our opinion, was a direct consequence of the processes described above.

Thus, the study results provide a rationale for the timely use of SHA in intensive therapy of toxic rhabdomyolysis to reduce the treatment duration in ICU and hospital [5, 10, 22, 29–33].

Conclusion

The use of selective hemoadsorption in patients with toxic rhabdomyolysis has significantly reduced the levels of endogenous intoxication markers such as myoglobin (by 70.7%) and CPK (by 94.4%) as well as the concentration of AKI markers such as cystatin-C (by 81.5%) by day 5 of treatment. This method was also associated with improved renal filtration starting from day 6 of treatment.

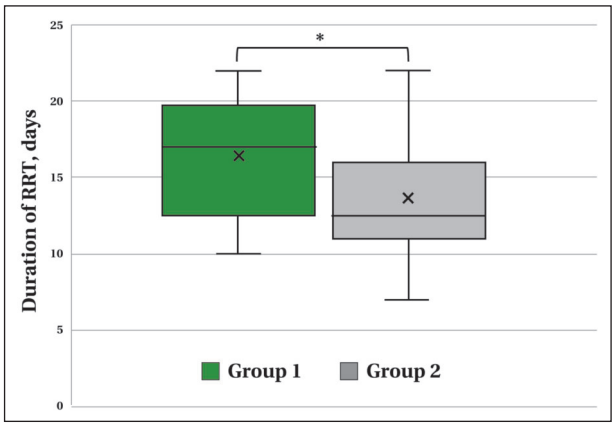

Fig. 3. Duration of RRT in the study groups.
Note. Data are presented as *Me* (*Q1*; *Q3*). * — significant differences between groups (Mann–Whitney *U*-test, $P<0.05$).

Early use of SHA reduced the length of stay in the ICU from 12 (7; 13) days to 7 (6; 9) days and in the hospital from 22 (14.5; 24.5) days to 12 (10; 16) days.

References

1. *Kolovou G., Cokkinos P., Bilianou H., Kolovou V., Katsiki N., Mavrogeni S.* Non-traumatic and non-drug-induced rhabdomyolysis. *Arch Med Sci Atheroscler Dis*. 2019; 4: e252–e263. DOI: 10.5114/amsad.2019.90152. PMID: 32368681.
2. *Chavez L.O., Leon M., Einav S., Varon J.* Beyond muscle destruction: a systematic review of rhabdomyolysis for clinical practice. *Crit Care*. 2016; 20 (1): 135. DOI: 10.1186/s13054-016-1314-5. PMID: 27301374.
3. *Safari S., Yousefifard M., Hashemi B., Baratloo A., Forouzanfar M.M., Rahmati F., Motamedi M., Najafi I.* The value of serum creatine kinase in predicting the risk of rhabdomyolysis-induced acute kidney injury: a systematic review and meta-analysis. *Clin Exp Nephrol*. 2016; 20 (2): 153–161. DOI: 10.1007/s10157-015-1204-1. PMID: 26801932.
4. *Petejova N., Martinek A.* Acute kidney injury due to rhabdomyolysis and renal replacement therapy: a critical review. *Crit Care*. 2014; 18 (3): 224. DOI: 10.1186/cc13897. PMID: 25043142.
5. *Хорошилов С.Е., Никулин А.В.* Патогенез, диагностика и эфферентное лечение рабдомиолиза, осложненного острой почечной недостаточностью. *Тверской медицинский журнал*. 2017; 5: 45–51. [*Khoroshilov S.E., Nikulin A.V.* Pathogenesis, diagnosis and efferent treatment of rhabdomyolysis complicated by acute renal failure. *Tver Medical Journal/Tverskoy Meditsinskiy Zhurnal*. 2017; 5: 45–51. (in Russ.).].
6. *Федорова А.А., Кутепов Д.Е., Зубарев А.В., Пасечник И.Н., Хабарина Н.В.* Рабдомиолиз: что нового в диагностике и лечении? *Кремлевская медицина. Клинический вестник*. 2020; 2: 102–109. DOI: 10.26269/4n94-0746. [*Fedorova A.A., Kutepov D.E., Zubarev A.V., Pasechnik I.N., Zabarina N.V.* Rhabdomyolysis: what's new in diagnosis and treatment? *Kremlin medicine. Clinical Bulletin/ Kremlevskaya meditsina. Klinicheskiy vestnik*. 2020; 2: 102–109. (in Russ.). DOI: 10.26269/4n94-0746.].
7. *Holt S., Moore K.* Pathogenesis of renal failure in rhabdomyolysis: the role of myoglobin. *Exp Nephrol*. 2000; 8 (2): 72–76. DOI: 10.1159/000020651. PMID: 10729745.
8. *Kodadek L., Carmichael Ii S.P., Seshadri A., Pathak A., Hoth J., Appelbaum R., Michetti C.P., Gonzalez R.P.* Rhabdomyolysis: an American Association for the Surgery of Trauma Critical Care Committee Clinical Consensus Document. *Trauma Surg Acute Care Open*. 2022; 7 (1): e000836. DOI: 10.1136/tsaco-2021-000836. PMID: 35136842.
9. *Масолитин С.В., Проценко Д.Н., Тюрин И.Н., Мамонтова О.А., Магомедов М.А.* Современный взгляд на применение методов экстракорпоральной детоксикации при рабдомиолизе (обзор). *Общая реаниматология*. 2022; 18 (3): 59–68. DOI: 10.15360/1813-9779-2022-3-59-68. [*Masolitin S.V., Protsenko D.N., Tyurin I.N., Mamontova O.A., Magomedov M.A.* Current view on the use of extracorporeal detoxification methods for the treatment of rhabdomyolysis (review). *General reanimatology/Obshchaya reanimatologya*. 2022; 18 (3): 59–68. (in Russ.). DOI: 10.15360/1813-9779-2022-3-59-68].

10. *Donati G., Cappuccilli M., Di Filippo F., Nicoletti S., Ruggeri M., Scrivo A., Angeletti A., La Manna G.* The use of supra-hemodiafiltration in traumatic rhabdomyolysis and acute kidney injury: a case report. *Case Rep Nephrol Dial.* 2021; 11 (1): 26–35. DOI: 10.1159/000507424. PMID: 33708797.
11. *Guzman N., Podoll A.S., Bell C.S., Finkel K.W.* Myoglobin removal using high-volume high-flux hemofiltration in patients with oliguric acute kidney injury. *Blood Purif.* 2013; 36 (2): 107–111. DOI: 10.1159/000354727. PMID: 24080745.
12. *Masakane I., Sakurai K.* Current approaches to middle molecule removal: room for innovation. *Nephrol Dial Transplant.* 2018; 33 (suppl_3): iii12–iii21. DOI: 10.1093/ndt/gfy224. PMID: 30281129.
13. *Weidhase L., de Fallois J., Haußig E., Kaiser T., Mende M., Petros S.* Myoglobin clearance with continuous veno-venous hemodialysis using high cutoff dialyzer versus continuous veno-venous hemodiafiltration using high-flux dialyzer: a prospective randomized controlled trial. *Crit Care.* 2020; 24 (1): 644. DOI: 10.1186/s13054-020-03366-8. PMID: 33176824.
14. *Cabral B.M.I., Edding S.N., Portocarrero J.P., Lerma E.V.* Rhabdomyolysis. *Dis Mon.* 2020; 66 (8): 101015. DOI: 10.1016/j.disamonth.2020.101015. PMID: 32532456.
15. *Dilken O., Ince C, van der Hoven B., Thijsse S., Ormskerk P., de Geus H.R.H.* Successful reduction of creatine kinase and myoglobin levels in severe rhabdomyolysis using extracorporeal blood purification (CytoSorb®). *Blood Purif.* 2020; 49 (6): 743–747. DOI: 10.1159/000505899. PMID: 32114569.
16. *Daum H.C., Schmidt B.M.W., Napp L.C.* Effects of hemoadsorption with cytoSorb during severe rhabdomyolysis. *Blood Purif.* 2021; 50 (2): 268–269. DOI: 10.1159/000508277. PMID: 32535606.
17. *Linden K., Scaravilli V., Kreyer S.F., Belenkiy S.M., Stewart I.J., Chung K.K, Cancio L.C., Batchinsky A.I.* Evaluation of the Cytosorb™ hemoadsorptive column in a pig model of severe smoke and burn injury. *Shock.* 2015; 44 (5): 487–495. DOI: 10.1097/SHK.0000000000000439. PMID: 26368927.
18. *Köhler T., Schwier E., Praxenthaler J., Kirchner C., Henzler D., Eickmeyer C.* Therapeutic modulation of the host defense by hemoadsorption with CytoSorb®-Basics, indications and perspectives — a scoping review. *Int J Mol Sci.* 2021; 22 (23): 12786. DOI: 10.3390/ijms222312786. PMID: 34884590.
19. *Stahl K., Rastelli E., Schoser B.* A systematic review on the definition of rhabdomyolysis. *J Neurol.* 2020; 267 (4): 877–882. DOI: 10.1007/s00415-019-09185-4. PMID: 30617905.
20. *Gupta A., Thorson P., Penmatsa K.R., Gupta P.* Rhabdomyolysis: revisited. *Ulster Med J.* 2021; 90 (2): 61-69. PMID: 34276082.
21. *Baeza-Trinidad R.* Rhabdomyolysis: a syndrome to be considered. Rabdomiólisis: un síndrome a tener en cuenta. [Article in English, Spanish]. *Med Clin (Barc).* 2022; 158 (6): 277–283. DOI: 10.1016/j.medcli. 2021.09.025. PMID: 34872769.
22. *Scharf C., Liebchen U., Paal M., Irlbeck M., Zoller M., Schroeder I.* Blood purification with a cytokine adsorber for the elimination of myoglobin in critically ill patients with severe rhabdomyolysis. *Crit Care.* 2021; 25 (1): 41. DOI: 10.1186/s13054-021-03468-x. PMID: 33509234.
23. *Perkoff G.T., Hill R.L., Brown D.M., Tyler F.H.* The characterization of adult human myoglobin. *J Biol Chem.* 1962; 237: 2820–2827. PMID: 14037297.
24. *Wood T.D., Chen L.H., White C.B., Babbitt P.C., Kenyon G.L., McLafferty F.W.* Sequence verification of human creatine kinase (43 kDa) isozymes by high-resolution tandem mass spectrometry. *Proc Natl Acad Sci U S A.* 1996; 93 (21): 12051. DOI: 10.1073/pnas.93.21.12051-c. PMID: 8876261.
25. *Zorova L.D., Pevzner I.B., Chupyrkina A.A., Zorov S.D., Silachev D.N., Plotnikov E.Y., Zorov D.B.* The role of myoglobin degradation in nephrotoxicity after rhabdomyolysis. *Chem Biol Interact.* 2016; 256: 64–70. DOI: 10.1016/j.cbi.2016.06.020. PMID: 27329933.
26. *Масолитин С. В. Проценко Д.Н., Тюрин И.Н., Мамонтова О.А., Магомедов М.А., Ким Т.Г., Яралян А.В.* Применение селективной гемоперфузии при лечении токсического рабдомиолиза, осложненного острым повреждением почек. *Вестник анестезиологии и реаниматологии.* 2022; 19 (1): 58–66. DOI: 10.21292/2078-5658-2022-19-1-58-66. [*Masolitin S. V. Protsenko D.N., Tyurin I.N., Mamontova O.A., Magomedov M.A., Kim T.G., Yaralyan A.V.* The use of selective hemoperfusion in the treatment of toxic rhabdomyolysis complicated by acute kidney injury. *Messenger of Anesthesiology and Resuscitation/Vestnik Anesthesiologii i Reanimatologii.* 2022; 19 (1): 58–66. (in Russ.). DOI: 10.21292/2078-5658-2022-19-1-58-66].
27. *Schrezenmeier E.V., Barasch J., Budde K., Westhoff T., Schmidt-Ott K.M.* Biomarkers in acute kidney injury — pathophysiological basis and clinical performance. *Acta Physiol (Oxf).* 2017; 219 (3): 554–572. DOI: 10.1111/apha.12764. PMID: 27474473.
28. *Pasala S., Carmody J.B.* How to use… serum creatinine, cystatin C and GFR. *Arch Dis Child Educ Pract Ed.* 2017; 102 (1): 37–43. DOI: 10.1136/archdischild-2016-311062. PMID: 27647862.

29. *Padiyar S., Deokar A., Birajdar S., Walawalkar A., Doshi H.* Cytosorb for management of acute kidney injury due to rhabdomyolysis in a child. *Indian Pediatr.* 2019; 56 (11): 974–976. PMID: 31729332.
30. *Kwiatkowska M., Chomicka I., Malyszko J.* Rhabdomyolysis — induced acute kidney injury — an underestimated problem. *Wiad Lek.* 2020; 73 (11): 2543–2548. PMID: 33454698.
31. *Масолитин С.В., Проценко Д.Н., Тюрин И.Н., Мамонтова О.А., Магомедов М.А., Ким Т.Г., Попов А.Ю.* Применение комбинированной экстракорпоральной детоксикации при лечении токсического рабдомиолиза, осложненного острым повреждением почек: одноцентровое проспективное рандомизированное исследование. *Вестник интенсивной терапии имени АИ Салтанова.* 2022; 2: 95–107. DOI: 10.21320/1818-474X-2022-2-95-107. [*Masolitin S.V., Protsenko D.N., Tyurin I.N., Mamontova O.A., Magomedov M.A., Kim T.G., Popov A.Yu.* The use of combined extracorporeal detoxification in the treatment of toxic rhabdomyolysis complicated by acute kidney injury: a single-center prospective randomized study. *Ann Crit Care/Vestnik Intensivnoy Terapii im A.I. Saltanova.* 2022; 2: 95–107. (in Russ.). DOI: 10.21320/1818-474X-2022-2-95-107].
32. *Lang C.N., Sommer M.J., Neukamm M.A., Staudacher D.L., Supady A., Bode C., Duerschmied D., Lother A.* Use of the CytoSorb adsorption device in MDMA intoxication: a first-in-man application and *in vitro* study. *Intensive Care Med Exp.* 2020; 8 (1): 21. DOI: 10.1186/s40635-020-00313-3. PMID: 32542550.
33. *Хорошилов С.Е., Никулин А. В.* Детоксикация при критических состояниях: понимание научной проблемы в XXI веке (обзор). Общая реаниматология. 2017; 13 (5): 85–108. DOI: 10.15360/1813-9779-2017-5-85-108. [*Khoroshilov S.E., Nikulin A.V.* Detoxification in critical conditions: an insight into the scientific problem in the XXI century (review). *General reanimatology/Obshchaya reanimatologya.* 2017; 13 (5): 85–108. (in Russ.). DOI: 10.15360/1813-9779-2017-5-85-108.].

Received 23.08.2022
Online First 07.12.2022