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Acute Kidney Injury in Patients With Acute Chemical Poisoning: the Experience of the Toxicological Center in Ryazan

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RELEVANCE Acute kidney injury (AKI) is one of the leading causes of death worldwide. However, the epidemiology of AKI is not well understood. In Russia, toxic kidney damage plays a significant role in the nosological structure of AKI — 12.2%.
AIM OF STUDY To study the features of AKI in patients with acute chemical poisoning.
MATERIAL AND METHODS We analyzed 26 case histories of patients with acute chemical poisoning with AKI (according to KDIGO). The comparison group included 25 patients with acute chemical poisoning without AKI. All patients were hospitalized in a toxicological center on the basis of the emergency department of the Ryazan Region State Budgetary Institution "City Clinical Emergency Hospital" (SBI RR "CCH EMC") in 2016–2018. The analysis of the annual reports of the chief toxicologist of the Ministry of Health of the Ryazan Region for 2016–2018 was carried out. Data processing was performed using Microsoft Office Excel 2013 and on the website medstatistic.ru (Pearson's chi-square test and Fisher's exact test).
RESULTS In most patients AKI developed during poisoning with cauterizing action substances - 38.4% (23% - vinegar essence, 15.4% - unidentified cauterizing action substance). The poisoning with alcohol substitutes (12%) took the 2nd place, with narcotic substances (8%) – the 3 rd place. Also, isolated cases of AKI (4% each) were reported in case of poisoning with pregabalin, tramadol, ketorol and ethanol. Poisoning with an unknown toxicant was noted in 29.6% of cases.
Most patients (69.2%.) had stage 3 AKI. The second stage was registered in 7.7% of patients, the first — in 23.1%. Proteinuria was detected in all patients who underwent common urine test (CUT). Infusion therapy using crystalloids was performed in 100% of cases.
CONCLUSION Acute renal injury most often develops in acute poisoning with cauterizing poisons. The development of acute kidney injury in acute chemical poisoning leads to an increased risk of death. Acute kidney injury is the second most common immediate cause of death in acute chemical poisoning. Infusion therapy is an integral part of the management of toxicological patients with acute kidney injury.
Keywords: poisoning, acute kidney injury, nephropathy, cauterizing agents
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INTRODUCTION

Acute poisoning is one of the main non-infectious causes of death in patients. More than 98% of poisoning occurs in everyday life, and in 60% of cases, the working-age population is affected [1].

According to the literature, in Russia the mortality rate in acute chemical poisoning reaches 17.2%. Acute chemical poisoning with alcohol-containing products is observed most often (32.1%) [2, 3].

Acute renal injury (AKI) is a pathological condition with a rapid development of renal dysfunction due to direct acute exposure to renal and / or extrarenal damaging factors. AKI is one of the leading causes of death worldwide. But, despite this, its epidemiology has been insufficiently studied [4].

According to the registry of renal replacement therapy of the Russian Federation, in our country toxic kidney damage (12.2% of all cases with known etiology) and acute interstitial nephritis (5.3%) play a significant role in the nosological structure of AKI. The mortality rate of patients with AKI in general is 27.3% [5].

Toxic nephropathy is a frequent pathological syndrome in acute exogenous poisoning. The main attention in the early diagnosis of toxic nephropathy is given to urinary syndrome. Careful measurement of urine output takes into account the ongoing infusion therapy and the possible loss of fluid by the extrarenal route [6].

Poisoning with cauterizing agents occupy the 3rd-4th place in the structure of hospitalizations (up to 7% of all patients with acute chemical poisoning). Toxic nephropathy is most common in acetic acid poisoning, occurring in

86.5% of patients with this pathology. The clinical manifestations of this type of nephropathy are different: from minor changes in the urine to the development of severe acute renal failure [7].

In Europe and the USA, poisoning with cauterizing agents in the general structure of acute poisoning occupies a negligible place: 0.4–0.5% of the total number of toxicological patients due to the absence of 70% of acid on sale [8].

Patients with chronic alcoholism are one of the groups at increased risk of developing acute chemical poisoning, including those accompanied by AKI. This is associated with frequent use of alcohol surrogates, as well as a higher suicidal potential [9].

Aim of study: to identify the features of AKI in acute chemical poisoning, as well as demonstrate the possibilities for managing such patients in a toxicological center operating on the basis of a city emergency hospital.

Objectives: to study the etiological structure, peculiarities of the course and outcomes of poisoning accompanied by the development of AKI (according to KDIGO), as well as the problems of diagnosis and treatment of AKI in these patients on the basis of the experience of a toxicological center based on the Emergency Department of the SBI RR "CCH EMC".

MATERIAL AND METHODS

We analyzed statistical cards of all patients with acute poisoning of the toxicological center on the basis of the emergency treatment department of the SBI RR "CCH EMC", as well as annual reports on toxicology of the chief toxicologist of the Ministry of Health of the Ryazan region for 2016–2018. Cards were selected indicating the following complications in the diagnosis: acute renal failure, hemoglobinuric nephrosis, nephropathy, AKI (38 cards). The corresponding medical histories of 26 patients were analyzed where AKI developed (in accordance with the KDIGO criteria). The comparison group included 25 patients with acute chemical poisoning without AKI. The analysis of associated documents to the acts of forensic medical examination of patients with AKI who died from acute poisoning was carried out. Statistical processing of the data was carried out using the Microsoft Office Excel 2013 software, as well as on the website medstatistic.ru using four-field tables (determination of the Pearson chi-square test and Fisher's exact test). The $p < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

When analyzing the case histories, it was revealed that AKI was indicated in the diagnosis in only one case out of 26 (4%). In most cases, the term "acute renal failure" was used (92%).

Among the patients with AKI included in the study, men predominated (22 people, 85%). The patients' age was from 22 to 72 years (mean age 44.4 ± 13.5 years). Among men, patients of young age (up to 44 years old inclusive) were more than half - 59.1%. The proportion of patients - middle-aged men was 27.3%; the elderly - 13.6%. The comparison group is represented by patients with acute chemical poisoning without AKI (25 people). The average age of patients in it was 42.8 ± 14.1 years, and 22 (88%) patients were men ($p > 0.05$).

The mortality rate among the patients with AKI included in the study reached 73%. In the comparison group, this figure was 16%. The difference in mortality in the group of patients with AKI from the same indicator in the comparison group was statistically significant, $p < 0.05$.

In most of the patients included in the study, AKI developed during poisoning with cauterizing agents - 38% (with a predominance of vinegar essence among them; $p < 0.05$).

In a third of cases, it was not possible to identify the toxic substance. One of the patients had a history of the use of antifreeze (Fig. 1).

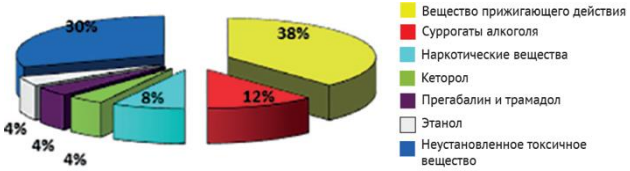

Fig. 1. Etiological structure of poisoning complicated by the development of acute kidney injury

In the structure of poisoning of patients in the comparison group shown in Fig. 2, ethanol poisoning prevailed - 48%. In second place in terms of frequency of occurrence in this group - drug poisoning (phenobarbital (8%), amitriptyline (4%) and phenazepam (4%)), in third place - narcotic substances (one case of poisoning (4% each) with methadone in combination with cocaine, heroin and pyrrolidinovalerophenone (PVP)). Also, the comparison group included 2 patients with poisoning with alcohol substitutes: isopropanol and methanol. Eight per cent of the total had the poisoning with a cauterizing substance (vinegar essence).

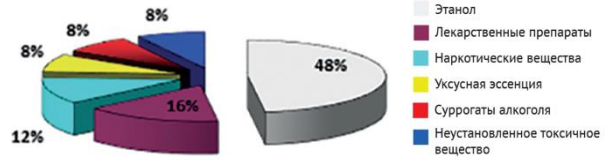

Fig. 2. Etiological structure of acute chemical poisoning in patients without acute kidney injury

In the general structure of chemical injuries, ethanol poisoning prevailed - 48.5%, poisoning with narcotic substances - 7.7%, with acetic acid - 2.6%, and other and unspecified substances - 3.7% were less common. The proportion of patients with AKI among all patients with poisoning was 1.5%. Attention is drawn to the fact that against the background of the general mortality in case of poisoning in 3.6%, AKI was observed in 23.8% of the deceased.

AKI most often developed in patients with vinegar essence poisoning (Fig. 3).

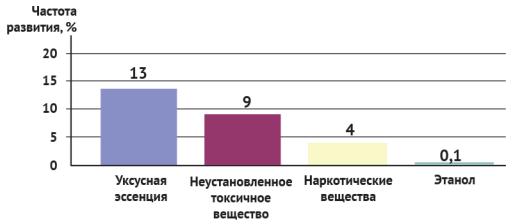

Fig. 3. The incidence of acute kidney injury in the most common poisoning

In 2017–2018, according to the toxicological center of the city of Ryazan, there is a decrease in the proportion of patients with AKI among deceased patients by 16% compared to 2016 (Fig. 4).

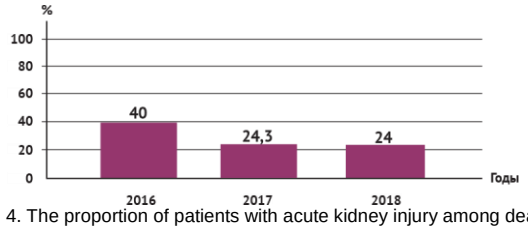

Fig. 4. The proportion of patients with acute kidney injury among deaths from acute chemical poisoning

The majority of patients with AKI were taken to the hospital by ambulance teams from home / from the street, 23% were referred from other hospitals.

The most frequent diagnosis of the referring institution was “poisoning with alcohol surrogates” (23.1%), somewhat less frequently patients were admitted with the diagnosis “vinegar essence poisoning” (19.2%), even less often - with poisoning with an unknown substance (7.7%) , methyl alcohol and ketorol (3.9% each). One of the patients was transferred from another hospital with pregabalin poisoning. Also, patients were identified who were referred to hospital with diagnoses of chronic alcohol intoxication, pneumonia and phenazepam poisoning (one case each). Some of the patients were admitted to the emergency department to exclude acute surgical pathology: acute pancreatitis (11.6%); thrombosis of mesenteric vessels, gastric ulcer (perforation) and gastric bleeding (3.9% each).

Patients with AKI were hospitalized mainly in the intensive care unit. Almost half of the patients were non-contact due to the severity of the condition.

The average value of the level of creatinine in the blood (maximum) in the group of patients with AKI was 561.5 ± 342.9 μmol/L; in the comparison group - 91.3 ± 18.2 μmol/L. The mean blood urea level was 32.5 ± 24.1 mmol/L in patients with AKI and 6.5 ± 2.5 mmol/L in patients without AKI. A decrease in urine output of less than 0.5 ml/kg/h for at least 6 hours was observed in 85% of cases of AKI. In 23.1%, AKI was diagnosed only in connection with a decrease or absence of diuresis, since the assessment of the creatinine level in dynamics was not performed (all patients were in the department for less than a day).

Most of patients had AKI stage 3 (Fig. 5).

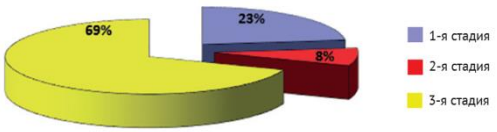

Fig. 5. The structure of the developed acute kidney injury by stages

Simultaneous development of four or more complications was registered in 88.5% of patients (Table 1).

Table 1

Other complications of acute chemical poisoning in patients with acute kidney injury

Complication	Incidence, %	Number of patients (*n*=26)
Cerebral edema	73.1	19
Encephalopathy	65.4	17
Acute respiratory failure	42.3	11
Pneumonia	38.5	10
Pulmonary edema	27	7
Intravascular hemolysis	27	7
Reactive pancreatitis	27	7
Acute stress-related erosions of Gi-tract	23.1	6
Toxic Hepatitis	19.2	5
Gastro-intestinal bleeding	15.4	4

The most frequent background condition in patients with AKI was chronic alcohol intoxication with multiple organ manifestations - 61.5% (in the comparison group this indicator reached 68%), drug addiction was less common - 19.2% (12% in the comparison group), p> 0.05. Concomitant chronic viral hepatitis C was registered in 19.2% of patients (16% in the comparison group), diabetes mellitus - in 15.4% (comparison group - 8%). Patients with arterial hypertension - 11.5% (comparison group - 20%). Patients with HIV infection (1 patient in the comparison group) appeared among the patients with AKI included in the study as often as patients with chronic pyelonephritis: 7.7% each, one of them had a history of urolithiasis. Among the patients of the comparison group, there were no patients with chronic pyelonephritis and urolithiasis.

According to the results of forensic medical examinations of the corpses of deceased patients, in all cases the clinical diagnosis coincided with the forensic one.

The most frequent immediate causes of death were: multiple organ failure (29.2%) and acute renal failure (25%) (Fig. 6).

Fig. 6. Immediate causes of death in patients with acute kidney injury according to a forensic study

Autopsy revealed necrotizing nephrosis in 17% of deceased patients with AKI (in 2 cases of acetic acid poisoning, one case of drug poisoning and an unidentified cauterizing agent). Also, 4% had pigmentary nephrosis (vinegar essence) and 4% had membranous glomerulopathy (with acetone poisoning).

The average length of hospital stay for AKI patients was 5.1 days. Moreover, many of them were in the department for no more than 2 days (46%). In one third of patients, the duration of hospital stay was up to 1 day. In all cases, such a short-term stay in the hospital was due to the initial severity of the patients' condition: deaths were observed in the first two days after hospitalization (p <0.05). The maximum hospital stay was 16 days.

AKI stage 1 was statistically significantly more often detected in patients who died on the first day of hospitalization (50%) than in patients who were in the department for more than 24 hours (11%, p <0.05).

The chemical and toxicological study of blood (with positive diuresis) was performed upon admission in all patients. In 23% of patients with AKI, blood tests revealed ethanol with the average content of 1.8 ± 1.1 g/L. In one case ethanol concentration was 3.8 g/L, and in the other cases - less than 3 g/L. In the comparison group, ethanol in the blood was found in 52% of patients, its average content was 4 ± 1 g/L. One patient with AKI (4%) had methanolemia - 302 mg%. Acetone in the blood of patients with AKI was found in 19.2% of cases, and in 4% of patients in a lethal concentration (63.8 mg%), the median of its content in the blood was 35.9 mg%. The chemical and toxicological study confirmed poisoning with ketorol, tramadol and ethylene glycol. In 50% of cases, the results of the chemical toxicological study were negative. In 2 patients with AKI, narcotic substances were found in the urine: codeine, heroin, desomorphine, levorphanol, dextromethorphan, respectively; morphine and methadone.

It should be noted that in the diagnosis of the majority of poisoning with cauterizing agents, chemical-toxicological research does not play a significant role, since it is not possible to determine the content of acid or alkali in biological fluids [7].

General urine analysis was performed in 77% of patients with AKI and 85% without it, microscopy of urine sediment was performed in AKI in 11.5% of cases (Fig. 7). In some cases, urinalysis was not performed for technical reasons. Proteinuria was detected in all patients with AKI who underwent general urinalysis. The median protein content in the morning urine portion in patients with AKI was 0.7 g/L, and in those without AKI - 0.034 g/L. In 27% of patients without AKI, proteinuria was not found.

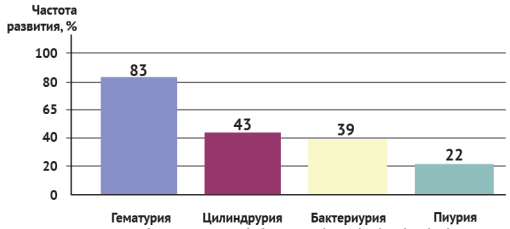

Fig. 7. Frequency and structure of detected pathological changes in urine sediment

The differences in the incidence of proteinuria with and without AKI were statistically significant ($p < 0.05$).

In the majority of patients, the level of potassium in the blood remained within the normal range (42.3%). Hyperkalemia as a concomitant AKI syndrome was observed in 26.9% of patients, and hypokalemia - in 15.4%. The average blood potassium level in AKI patients was 5.7 ± 1.7 mmol/L. Its average value in the comparison group was 4.2 ± 1.3 mmol/L. In 15.4% of cases with AKI, it was not possible to determine the level of electrolytes in the blood due to the short duration of the patient's stay in the department ($p < 0.05$).

Ultrasound examination of the kidneys, performed in almost all patients with AKI, in most cases did not reveal any abnormalities. An increase in the size of the kidneys (length and width) was found in 12.5% of patients, and an increase in the thickness of the parenchymal layer was found in 8.5%.

According to the authors, acute kidney injury is the second most common direct cause of death from poisoning.

All patients with AKI underwent infusion therapy, most often with the use of crystalloids (0.9% sodium chloride solution in 100% of cases; 5% glucose solution in 73%, Ringer's solution in 35% and Hartman's solution in 31%). Reamberin was used in 69.2% of cases. Loop diuretics (intravenous furosemide) were administered in 73% of cases (19 patients). Moreover, in 37% of cases they were used in patients with pulmonary edema, in 34% - with arterial hypertension and / or the presence of peripheral edema, and in 29% - after elimination of arterial hypotension. In the comparison group, the frequency of use of furosemide was only 20%, in all cases it was prescribed with the development of pulmonary edema (the difference in the frequency of use compared to that in patients with AKI is statistically significant, $p < 0.05$). According to clinical guidelines, the use of diuretics in AKI with oliguria / anuria in order to restore urine output is justified only in the presence of signs of hypervolemia; in other cases, diuretics should be avoided. It follows from this that in 29% of cases of furosemide use in patients included in the study, it was optimal to refuse its administration. However, it is worth noting its use in this situation in minimal doses (20-40 mg, and only once).

In 80% of cases, B vitamins were prescribed (infusion), the same proportion of patients received antibiotic therapy (ceftriaxone), sometimes combined. Antibiotics were used in patients with pneumonia, as well as in all poisoning with cauterizing agents. Eufillin was used intravenously in 85% of patients in order to stimulate diuresis and / or as one of the components of complex therapy for respiratory failure, if any. More than half of the cases were accompanied by hepatoprotection with ademetionine, 15.4% - with Remaxol. Almost half of the cases were infused with vasopressors, potassium chloride and calcium chloride.

Renal replacement therapy was performed in 4 patients (in 3 cases by veno-venous hemodiafiltration using hemodiafilter AV600 Fresenius; in one case - after transfer to another medical institution, hemodialysis department). Mortality in this group of patients was 75%. In 100% of cases, renal replacement therapy was performed according to absolute indications (when the level of urea in the blood was over 35.7 mmol/L or with hypervolemia insensitive to diuretics). Relative indications for its implementation were identified in 88.5% of patients.

Infusion therapy for detoxification purposes, regardless of the presence of AKI, is carried out in all patients with acute oral chemical poisoning. This explains why it was carried out in 100% of patients included in the study. It should be noted the use of crystalloids in all cases of persistent arterial hypotension. It is with them, according to clinical guidelines, that AKI therapy should be started in hypoperfusion (prerenal AKI mechanism). The use of "renal" doses of dopamine for the purpose of nephroprotection in critically ill patients with AKI is ineffective according to current data [4].

Renal replacement therapy in patients included in the study was carried out only according to absolute indications; expanding the possibilities of its use in a city hospital should be considered as a promising task.

In general, AKI can be treated with any renal replacement therapy available at a particular hospital [4]. In the conditions of SBI RR "CCH EMC", it was possible to carry out only veno-venous hemodiafiltration.

In the laboratory of the SBI RR "CCH EMC" the parameters characterizing hemolysis, the level of magnesium in the blood and the pH of the blood are not measured. The use of other methods of renal replacement therapy in addition to veno-venous hemodiafiltration at the time of the study was possible only in the hemodialysis department of another city clinical hospital, with a transfer presenting some difficulties.

CONCLUSION

1. Acute kidney injury is the second most common cause of immediate death in acute poisoning.
2. Most often (38%) acute renal injury developed in patients with poisoning with cauterizing agents.
3. In the majority of patients (69%), acute stage 3 renal injury developed.
4. The emergence of acute kidney injury in acute chemical poisoning leads to an increased risk of death (mortality in the group of patients with AKI is 73%, and in the control group - 16%, the differences between them are statistically significant).

5. Acute kidney injury of the 1st stage was statistically significantly more often detected in patients who died during the first 24 hours of hospital stay than in patients who were in the department for more than 24 hours (50% and 11%, respectively).

6. The complex of therapy for all toxicological patients with acute kidney injury in the absence of contraindications should include infusion therapy with 0.9% sodium chloride solution.

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