

Advanced Prediction of Acute Renal Damage in Patients with Polytrauma (Combined Trauma)

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Abstract

The purpose of the study was to determine the early diagnostic criteria for acute renal damage in patients with combined trauma by introducing a cystatin C serum biomarker into the survey plan for the affected patients.

Materials and Methods: The study of 42 patients received combined trauma from 2015 to 2016 was carried out. The biomaterial for determining the level of cystatin C was serum of blood. The blood sampling was carried out at 1-st, 3-rd, 7-th, 14-th days from the time of trauma. Men predominated among the aggrieved (80%), who were 4 times more than women. The Reberg-Tareev test was used to assess the filtration - reabsorption function of the kidneys. For the all patients from the group of examined were determined the following indicators: the blood creatinine, the creatinine of urine, urine quantity per 1 hour, minute diuresis, glomerular filtration, tubular reabsorption, amount of allotted urine per day.

Results and Discussion: In the course of the survey, it was revealed that in 40 (95.3%) patients, the Reberg-Tareev test was within normal limits. Whereas in 2 (4.7%) the indicators were below the normative values, which was associated with the development of a clinic for acute renal failure. In 2 examined patients the acute renal failure developed on the sixth to seventh day after an injury. The glomerular filtration rate was determined by the Reberg-Tareev test and by cystatin C. In the course of the study, it was revealed that the overwhelming majority of patients with combined trauma had a normal level serum creatinine (38 people). The level of cystatin C serum in 33 (78.6%) of the aggrieved more than 30% had higher than the normal values. At that, an increase in the level of cystatin C was observed in the first 3 days, then the gradual decrease of his occurred. The glomerular filtration rate according to the Reberg-Tareev test was reduced only in 4 patients, while in the calculation according to the Hawke formula, it was affected in 33 patients. From the 42 patients on the third day from the moment of trauma in 12, based on an increase in the serum cystatin C in the 0.92-2 mg /1 range - 19-49 years and 1.02-2 mg /1 -> 50 years, was diagnosed subclinical acute kidney damage. Wherein, the parameters of azotemia in this group of patients were within the norm. The based on the above data, it is seen that the glomerular filtration rate is reliably lower in serum cystatin C than in serum creatinine, which indicates a hidden renal dysfunction and subclinical acute kidney damage.

Keywords: combined trauma; cystatin C; acute renal failure; Glomerular Filtration Rate;

Introduction

The problem of patients' early diagnosis of acute renal damage with combined trauma is one of the major problems of clinical medicine, unfortunately, is still under development. Many issues of diagnosis and treatment are still unresolved and studies of early clinical and diagnostic features of acute renal damage in patients with combined trauma will enable timely and accurate diagnosis of impaired renal function and choose the right treatment tactics.

Nowadays, various biomarkers have been searched in clinical practice that would allow early diagnosis of acute renal damage, with their subsequent inclusion in the study algorithm [4]. Such markers in the serum are cystatin C, NGAL, atrial sodium -uretic peptide, CD 11b-neutrophil. Parameters of the urinary tract in urine are an increase in the level of NGAL, IL-18, kidney damage-1, LDH, N-acetyl-glucosaminidase, matrix metalloproteinase 9 [5,6].

Since the glomerular filtration rate is the most reliable indicator that reflects the functioning of the kidneys, it is especially relevant to search for an accurate, simple, low-traumatic and rapid method for determining GFR in victims with a combined trauma. Determination of serum cystatin C is a relatively new method for evaluating GFR [1, 7, 11]. Cystatin C is the most reliable indicator of the preservation of kidney function, it is a more sensitive indicator of reducing GFR than serum creatinine, which makes it possible to consider it an effective criterion for diagnosis of OPP even at normal values of serum creatinine [2,12]. The rate of production of cystatin C, unlike creatinine, is not affected by factors such as age, muscle mass, sex, eating habits, inflammatory reactions in the body [9,11,15,20,21].

The purpose of the study was to determine the early diagnostic criteria for acute renal damage in patients with combined trauma by introducing a cystatin C serum biomarker into the survey plan for the affected patients.

Materials and Methods

A prospective study with a practical purpose was conducted. The clinical study conducted by the department of faculty and endoscopic surgery of Kabardino-Balkarian State University is based on the department of combined trauma of the republican clinical hospital. A study of 42 patients who received a combined trauma for the period from 2015 to 2016 was carried out. Patients with respect to the main anthropometric criteria and social parameters by groups did not statistically significantly differ. The severity of the patients did not differ significantly.

All included patients signed informed consent before collecting any information for the study. The original of the signed informed consent was kept by the researcher. The second copy was given to the patient. The form of the informed study and the protocol of the clinical study were approved by the local ethics committee and the scientific council of the clinic of Kabardino-Balkarian State University in accordance with local regulatory requirements prior to the start of the study.

The biomatrix for determining the level of cystatin C was serum. Blood sampling was performed at 1.3, 7.14 days from the time of injury.

The overwhelming number of victims 39 (92.8%) were from 21 to 60 years, i.e. in the most able-bodied age, which is important from the standpoint of medical and social rehabilitation. Among the victims, men predominated (80%), who were 4 times more than women.

The data obtained during the study were processed by the variational-statistical method according to Student’s t-criterion. The arithmetic mean (x), the standard deviation (Dx), the standard error of the mean value (a) are calculated. The data are presented in the form $Ax + o$, and also n is the number of subjects. Differences in the data obtained were considered reliable if the significance level was $p < 0.05$, which is a measure of sufficient reliability in medical research [10]. A statistical analysis package and built-in calculation formulas for the Microsoft® Excell computer program (Microsoft Office 2010) were also used.

To evaluate the filtration - reabsorption function of the kidneys, the Reberga - Tareev test was used. This method allows you to determine the purifying ability of the kidneys, based on the definition of renal clearance of exogenous creatinine. All the patients from the group of subjects were assessed by the following indicators: blood creatinine, urine creatinine, urine quantity per 1 hour, diuresis, glomerular filtration, tubular reabsorption, amount of urine excreted per day.

Results

In the course of the survey, it was found that in 40 (95.3%) patients, the Reberg-Tareev test was within normal limits. Whereas in 2 (4.7%) the indicators were lower than the normative values, which was associated with the development of a clinic for acute renal failure.

In 2 of the examined patients, on the sixth to seventh day after an injury, acute renal failure developed. The test of Reberg-Tareev was performed before the development of the oliguric stage.

Recall that this group of patients was conducted a parallel determination of serum cystatin C in blood. Blood sampling for the concentration of serum cystatin C was carried out at 1.3.7, 14 days from the time of injury. The glomerular filtration rate was determined by the Reberg-Tareev test and by the cystatin C sample. Since we used the DiaSys CystatinC FS reagent, the calculation of GFR was performed according to the Hawke equation: $GFR [ml / min / 1.73 m^2] = (80.35 / cystatin C [mg / l]) - 4.32$. I would like to note that the study group of patients in the history of chronic kidney disease was not. The normal values of serum cystatin C are: 19-49 years - 0.53-0.92 mg / l; > 50 years - 0.58-1.02 mg / l.

Based on the clinical application of this method of diagnosis of acute renal damage and subclinical acute renal damage in patients with combined trauma, we developed diagnostic criteria for these pathological conditions. When serum cystatin C was obtained in the range of 0.92-2 mg / L (19-49 years) and 1.02-2 mg / L (> 50 years), we were diagnosed with subclinical acute renal damage, which was also confirmed by the absence of clinical symptoms. When obtaining a cystatin C level in the blood serum exceeding 2 mg / l in both age groups, we diagnosed acute renal damage, the clinic of which was clearly pronounced.

The study revealed that the vast majority of patients with combined trauma had a normal serum creatinine level (38 people). The level of serum cystatin C in 33 (78.6%) of the victims was more than 30% higher than the normal values. Moreover, an increase in the level of cystatin C was observed in the first 3 days, then a gradual decrease occurred.

As an example in a particular patient (K.47 years) of the initial degree of increase and dynamics of serum cystatin C: [Table 1] [Figure 1].

Table 1: Dynamics of serum cystatin C level patient K. 47 years old with severe combined trauma

Days of fixing	1 day	3 days	5 days	1 week	2 weeks
Cystatin C serum level	1.1 mg/l	1.7 mg/l	1.45 mg/l	1.3 mg/l	0.88 mg/l



Figure 1: Change in serum cystatin C level in dynamics by the example of a patient with severe combined trauma K.47 years

In 7 (21.2%) of those examined with elevated cystatin C levels, the high numbers were preserved and 1 week after the injury was received. Among the examined patients, 24 patients had a kidney injury, 15 (62.5%) of which the cystatin C values were higher than normal. In 1 patient, 1 month before the injury after a nephrectomy on the left, the level of cystatin C also exceeded the normal values (1.4 mg / l).

The glomerular filtration rate according to the Reberg-Tareev

test was only reduced in 4 patients, whereas in the calculation by the Hawke formula, 33 patients were affected.

Of the 42 survey sample on the third day after the trauma in 12, based on an increase in serum cystatin C in the 0.92-2 mg / l range - 19-49 years and 1.02-2 mg / L -> 50 years, it was diagnosed subclinical acute renal damage. At the same time, the parameters of azotemia in this group of patients were within the norm. [Table 2]

Table 2: Summary table of serum cystatin C, creatinine, SKF injured, who developed acute subclinical damage to the kidney for 3 days.

No	Serum cystatin C, mg/l	GFR (Ser. Cys. C, ml/min/l)	Serum creatinine mkmol/l	GFR (creatin) ml/min/l	No	Serum cystatin C, mg/l	GFR (Ser. Cys. C, ml/min/l)	Serum creatinine mkmol/l	GFR (creatin) ml/min/l
1	1,34	55,6	89	95	7	1,9	37,9	119	65
2	1,42	52,2	93	91	8	1,68	43,5	115	68
3	0,96	79,3	84	100	9	1,59	46,2	100	76
4	1,00	76,0	102	76	10	1,65	44,4	88	90
5	0,98	77,6	ΠΟ	68	11	1,73	42,1	86	95
6	1,58	46,5	115	65	12	1,84	39,3	116	68

Based on the above data, it can be seen that the glomerular filtration rate is significantly lower in serum nystatin C than in serum creatinine, which indicates a latent renal dysfunction, subclinical acute renal damage. Thanks to the early medical and preventive measures, 10 patients with combined trauma managed to prevent the development of acute kidney damage. In two, subclinical acute kidney damage passed into OPP, serum cystatin C on days 5 and 7 was above 2 mg / ml (2.6 mg / L and 2.75 mg / L, respectively).

Nephroprotective therapy was carried out with N-acetylcysteine (N-AC), which was prescribed in a standard dose: 1200 mg intravenously struino after admission to hospital and surgical treatment, then 600 mg intravenously twice a day for 72 hours, then inside 600 mg 2 times a day for 10 days. After discharge from the hospital, patients were given a second course

of N-acetylcysteine treatment once every 3 months at a dose of 1200 mg per day for 14 days.

The antioxidant N-AC binds free radicals that cause a lot of damage, including damage to the kidney tubules. Also N-AC interacts with the endothelium, acting as a relaxing factor, thereby increasing capillary blood flow. In addition, N - AC increases the level of c HMP, acts as a vasodilator and as an inhibitor of platelet aggregation. All of the above provides a nephroprotective effect of N-AC in the perioperative period in patients with a combined trauma, which is confirmed by a low serum cystatin level. N-AC reduces the severity of the inflammatory reaction in the body and thereby reduces the secretion of plasma cystatin C followed by its complete metabolism in the kidneys [8,13,14,16,17,18,19]. During the treatment, the filtration capacity of the kidneys was monitored in patients with combined trauma (Table 3, Figure 2).

Table 3: Comparative dynamics of changes in plasma cystatin C and creatinine concentration, GFR during treatment in the main group

Time of fixing indicators	Mean values of serum Cystatin C (n = 42), mg / L *	Mean values of serum creatinine, $\mu\text{mol} / \text{L}^*$	GFR for cystatin C, ml / min / 1.73 m ²	GFR for creatinine, ml / min / 1.73 m ²
1 day	2,4±0,7	97±14,5	29,2	94,5
3 days	2,2±0,7	123±5,7	32,2	66,8
7 days	1,5±0,5	137±6,2	49,2	60,3
14 days	0,82±0,1	111±16,2	93,6	73,8
21 days	0,73±0,1	92±13,3	105,7	103,5

Note: * - p <0.05; GFR - glomerular filtration rate

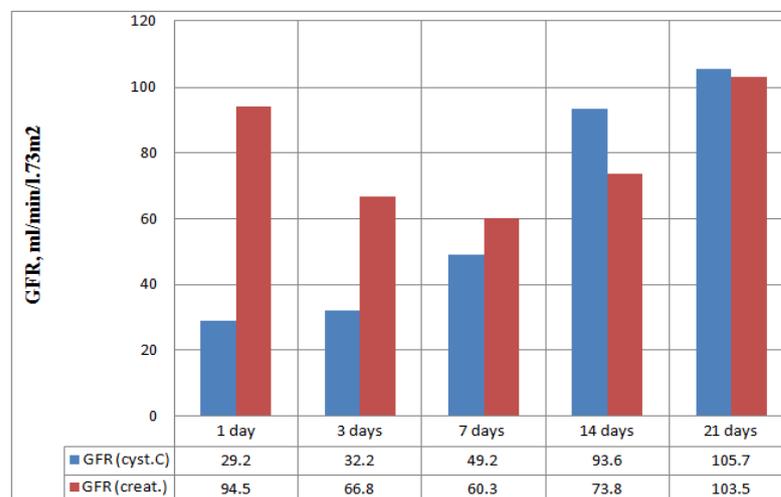


Figure 2: Comparative dynamics of the Glomerular Filtration Rate (GFR) for serum nystatin C and plasma creatinine

Discussion

It should be noted that, in contrast to blood creatinine, serum cystatin responded with an increase in concentration on the first day after the injury, while hypercreatininaemia was observed only by 3 days of observation. The rate of glomerular filtration, calculated by the Hawke formula, decreased in the first day and recovered by 2 weeks. When calculating the GFR by the Reberg-Tareev test, the decrease was noted to 3 days after the injury. This again confirms that the creatinine of blood is unreliable for a number of reasons, one of which is to increase its level with already developed renal damage [3].

In connection with the low information content of serum creatinine as an indicator of GFR, the diagnostic value of the original marker, cystatin S, was determined in this study. The most important advantage of cystatin C in comparison with creatinine in determining GFR is that it is able to identify the victims even with slightly impaired renal function, so as it has more specificity and sensitivity. We believe that the results of this study will be important in the early diagnosis of acute renal damage in patients with combined trauma. The use of the determination of the serum biomarker cystatin C in the first hours after injury will allow early diagnosis of renal dysfunction in patients with combined trauma.

Conclusions

1. The inclusion of the determination of serum concentration of cystatin C in the diagnosis of renal dysfunction in patients with combined trauma in the study panel is more preferable in comparison with creatinine.
2. It has been established that the glomerular filtration rate calculated from serum cystatin C (Hawke's formula) is the most reliable in comparison with GFR in the Reberg-Tareev test.
3. Serum concentration of cystatin C in the range of 0.92-2 mg / l (19-49 years) and 1.02-2 mg / l (> 50 years) may be a marker of subclinical acute renal damage without a clinical symptom.
4. Using the literature data, the role of N-acetylcysteine in a complex of conservative measures for the prevention and treatment of acute renal damage in patients with combined trauma was discussed.

Information on Funding and Conflict of Interest

The study did not have sponsorship. The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article.

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