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JOURNAL	World Science
p-ISSN	2413-1032
e-ISSN	2414-6404
PUBLISHER	RS Global Sp. z O.O., Poland
ARTICLE TITLE	DYNAMICS C-REACTIVE PROTEIN AND CERULOPLASMIN IN THE BLOOD OF PATIENTS WITH COMBINED THORACIC TRAUMA AS A PROGNOSTIC CRITERION OF TRAUMATIC DISEASE
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ARTICLE INFO	Boiko Olena, Volkova Yuliya. (2021) Dynamics C-Reactive Protein and Ceruloplasmin in the Blood of Patients with Combined Thoracic Trauma as a Prognostic Criterion of Traumatic Disease. World Science. 1(62). doi: 10.31435/rsglobal_ws/30012021/7404
DOI	https://doi.org/10.31435/rsglobal_ws/30012021/7404
RECEIVED	16 November 2020
ACCEPTED	17 January 2021
PUBLISHED	22 January 2021
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DYNAMICS C-REACTIVE PROTEIN AND CERULOPLASMIN IN THE BLOOD OF PATIENTS WITH COMBINED THORACIC TRAUMA AS A PROGNOSTIC CRITERION OF TRAUMATIC DISEASE

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DOI: https://doi.org/10.31435/rsglobal_ws/30012021/7404

ARTICLE INFO

Received: 16 November 2020

Accepted: 17 January 2021

Published: 22 January 2021

KEYWORDS

combined thoracic trauma,
C-reactive protein, ceruloplasmin
intensive care.

ABSTRACT

Purpose: to assess the informativeness of the level of "acute phase" proteins in the blood and their changes in the acute and early period of traumatic disease in patients with combined thoracic trauma with polytrauma as a marker of disease severity and the impact of proposed modifications of intensive care algorithm on treatment results.

Material and methods. The basis of this study is a statistical analysis of the results of a comprehensive examination of 92 patients with thoracic trauma. Control points were 1st, 2nd, 3rd, 5th, 7th and 12th day of treatment. The severity of the injury was determined according to the ISS scale, the condition of patients at the time of admission according to the ARASNE II scale, the level of C-reactive protein and ceruloplasmin in the blood. 3 groups of patients were identified. Group I - standard IT protocol, group II - standard IT protocol with the addition of ceruloplasmin, group III - standard IT protocol with the addition of a solution of D-fructose-1,6-diphosphate sodium salt of hydrate. Parametric statistics methods were used to process the obtained data.

Results. In patients with combined thoracic trauma, it is important when planning the patient's management tactics to diagnose the content of CRP and CP in the blood during the entire period of stay in the intensive care unit. The level of CP in the blood of patients with combined thoracic trauma is a highly informative diagnostic marker of the impact of hypoxia of mixed genesis on the course of traumatic disease in general. The leading mechanism for the development of acute lung injury syndrome in patients with combined thoracic trauma is oxidative stress, so the appointment of ceruloplasmin as an adjunct to the standard protocol of intensive care is pathogenetically justified.

Conclusions. In patients with combined thoracic trauma, it is important when planning patient management tactics to diagnose the content of C-reactive protein and ceruloplasmin in the blood during the entire period of stay in the intensive care unit. The level C-reactive protein and ceruloplasmin in the blood of patients with combined thoracic trauma is a highly informative diagnostic marker of the prognosis. There is oxidative stress, so the appointment of ceruloplasmin as an adjunct to the standard protocol of intensive care is pathogenetically justified.

Citation: Boiko Olena, Volkova Yuliya. (2021) Dynamics C-Reactive Protein and Ceruloplasmin in the Blood of Patients with Combined Thoracic Trauma as a Prognostic Criterion of Traumatic Disease. *World Science*. 1(62). doi: 10.31435/rsglobal_ws/30012021/7404

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Introduction. A feature of injuries in recent decades is the increase in the severity of injuries and changes in their structure [1, 2]. The proportion of polytrauma has significantly increased, reaching 5.5-35% according to various authors [3, 4]. The structure of polytrauma is very variable and depends on many factors. One of the most difficult options for the course of traumatic illness is a

combined thoracic injury [5, 6]. Its complicated course occurs in 36.8-75.5% of cases [7]. In this case, the main factors contributing to the development of complications are blood loss with a deficit of circulating blood volume of more than 40%, severe damage to the chest, accompanied by aspiration-regurgitation syndrome, cardiovascular dysfunction, and prolonged ventilation [8, 9].

Currently, for the diagnosis of respiratory distress syndrome, which often accompanies combined thoracic trauma, many clinical, laboratory, instrumental and morphological indicators have been proposed to assess the nature of disorders of external respiration, lung biomechanics, determine the nature and extent of lung tissue damage, aero hematic barrier, etc. [10, 11]. Given that multimarker panels are used at the current level to identify and predict the manifestations of acute lung injury syndrome, it is important to find their undefined components primarily in patients with combined thoracic trauma [12, 13]. According to the electronic databases MEDLINE and EMBASE for the last 10 years no information was found on the role of C-reactive protein (PSP) as an "acute phase" protein and its changes under the influence of different pathogenetic effects on the course of mixed hypoxia - exogenous ceruloplasmin (CP) and D-fructose-1,6-diphosphate sodium salt hydrate - in the interpretation of the prognosis in this category of patients, which justified the purpose of this study.

Given that the increase in "acute phase" proteins - PSA - in combined thoracic trauma indicates the development of an inflammatory reaction, and an increase in ceruloplasmin indicates the activation of the body's own antioxidant system in hypoxia and tissue ischemia, it is important to determine their blood levels and correlations during the course of traumatic illness as a criterion for maintaining homeostasis.

The aim of the study was to evaluate the informativeness of blood levels of "acute phase" proteins and their changes in acute and early traumatic disease in patients with combined thoracic trauma with polytrauma as a marker of disease severity and the impact of proposed modifications of intensive care algorithm on treatment outcomes.

Materials and methods. This study is based on a statistical analysis of the results of a comprehensive examination of 92 patients with thoracic trauma who were treated in the polytrauma department of the Municipal Non-Profit Enterprise "Clinical Hospital of Ambulance and Emergency Care named after prof. O. I. Meshchaninov" Kharkiv City Council in the period 2017-2019. Ethical aspects of the work were approved at the meeting of the Commission on Biomedical Ethics of the Kharkiv National Medical University of the Ministry of Health of Ukraine (Protocol № 9 of 21.09.2017). All patients signed an informed consent to participate in the study.

The effectiveness of the proposed methods of treatment in the process of cohort clinical open prospective study in the division of patients into 3 stratified groups was evaluated. Randomization was performed by the method of "envelopes".

Group I included 30 patients with combined thoracic trauma, who received intensive care (IC) of the received injuries according to the unified clinical protocol of emergency medical care of the Ministry of Health of Ukraine "Polytrauma" (2016).

Group II included 30 patients with combined thoracic trauma, who in addition to the main IC protocol was prescribed a solution of ceruloplasmin in a daily dose of 6 mg/kg diluted in 200 ml of 0.9% sodium chloride solution at a rate of 30 drops per minute intravenously during the first week hospital stay.

Group III included 32 patients with combined thoracic trauma, who in addition to the main IC protocol was prescribed a solution of D-fructose-1,6-diphosphate sodium salt hydrate intravenously in a dosage of 150 mg/kg of ideal body weight 2 times a day (after 12 hours) at a rate of 10 ml per minute during the first 7 days of treatment.

Verification of the diagnosis of thoracic trauma and its dynamics was established on the basis of clinical and anamnestic features, radiographic data, determination of blood gas composition. The severity of injuries of the anatomical areas was determined using the ISS scale (Injury Severity Score), the degree of pulmonary damage in the dynamics was assessed by the LIS scale (Lung Injury Score), the determination of the ARF stage was performed according to the classification of V.L. Cassil (1997). In patients with intrapleural trauma, studies were performed after evacuation of the latter.

Criteria for inclusion in the study: age up to 60 years, the presence of lung damage in polytrauma, the possibility of productive contact with the patient at admission (14-15 points for SCG), obtaining informed consent, no history of blood diseases, cancer, COPD, bronchial asthma, aggravated heredity, alcoholism, mental disorders, allergic reactions, blood transfusions, moderate severity of

injuries (9-24 points on the ISS scale), the number of points on the ARACHE II scale at the time of admission no more than 10 points, lack of inotropic support in the prehospital stage.

Criteria for non-inclusion in the study: age over 60 years, the presence of damage to the craniofacial anatomical and functional area, as well as abdominal organs, musculoskeletal system on the scale of severity (AIS), which belonged to the category "trauma is critical, survival is unlikely", the presence of post-traumatic heart attack.

To analyze the dynamics of the traumatic disease in patients, control points were selected - 1st, 2nd, 3rd, 5th, 7th and 12th of hospital stay. This was due to the fact that, despite the absence of severe injuries - 9-24 points on the ISS scale, up to 10 points on the ARACHE II scale - the presence of combined injuries in the presence of thoracic trauma increases the likelihood of acute lung injury syndrome, the period of development of which in most cases coincides with the first week of the traumatic disease [12].

Blood for the study in patients was taken on an empty stomach at 8.00 am on the appropriate day. The study of CRP concentration was performed by the quantitative method of immunoturbidimetry according to OP Shevchenko (1997). The level of CP was determined by a modified method of Revin, based on the oxidation of p-phenylenediamine, with the participation of ceruloplasmin with stopping the reaction with sodium fluoride solution (Babenko GO, 1999).

Statistical data processing was performed on a personal computer. Verification of the significance of the obtained data, which were previously entered into Excel spreadsheets, was carried out using Student's t-test (for $n < 100$) at a given level of reliability $p = 0.05$, for the possibility the use of Student's criterion introduced the Bonferroni amendment.

Results of the research

In the study of the dynamics of the level of PSA and CP in the studied patients, the following data were found (table 1, 2).

Table 1. Dynamics of the level of C-reactive protein in the studied patients, mg / l, ($M \pm \sigma$)

Day	Groups		
	Group I, n = 30	Group II, n = 30	Group III, n = 32
1	10,0 \pm 6,6	4,9 \pm 2,5	3,6 \pm 1,9
2	57,3 \pm 32,4	31,4 \pm 17,8	39,5 \pm 14,2
3	80,0 \pm 31,9	44,3 \pm 24,9	56,5 \pm 27,4
5	96,9 \pm 28,7	26,1 \pm 15,6 ^{*1,2}	64,7 \pm 24,4
7	87,6 \pm 32,1	22,2 \pm 11,7 ^{*1,2;*2,3}	68,8 \pm 31,2
9	76,5 \pm 29,1	16,3 \pm 7,3 ^{*1,2;*2,3}	47,8 \pm 17,7
12	52,0 \pm 21,4	12,0 \pm 4,1 ^{*1,2;*2,3}	34,8 \pm 8,2

Note: ^{*1,2} - $p < 0,05$ - probable difference between the groups I i II; ^{*2,3} - $p < 0,05$ - probable difference between the groups II i III.

Table 2. Dynamics of ceruloplasmin level in the studied patients, mg / l, ($M \pm \sigma$)

Day	Groups		
	Group I, n = 30	Group II, n = 30	Group III, n = 32
1	269,7 \pm 17,2	253,6 \pm 16,3	260,1 \pm 17,0
2	300,3 \pm 40,3	264,7 \pm 18,5	283,3 \pm 24,3
3	311,4 \pm 46,2	269,9 \pm 20,8	290,1 \pm 32,6
5	332,6 \pm 42,0	273,3 \pm 12,6 ^{*1,2}	298,4 \pm 35,3
7	319,5 \pm 31,4	265,1 \pm 13,6 ^{*1,2}	288,4 \pm 33,2
9	317,7 \pm 24,9	264,5 \pm 10,5 ^{*1,2}	274,7 \pm 19,6
12	303,4 \pm 14,1	260,0 \pm 13,5 ^{*1,2}	267,7 \pm 12,1 ^{*1,3}

Note: ^{*1,2} - $p < 0,05$ - probable difference between the groups I i II; ^{*1,3} - $p < 0,05$ - probable difference between the groups II i III.

Given the fundamentally different effects on the processes occurring in the body under the influence of hypoxia of mixed genesis in combined thoracic trauma, additional pharmacological substances - ceruloplasmin solution in patients of group II and solution of D-fructose-1,6-diphosphate sodium salt hydrate in patients of group III, it is important to monitor the dynamics of the level of CRP and CP in the blood of the studied patients. Thus, when conducting a statistical analysis of the dynamics of PSA levels, which characterizes the state of inflammatory processes in the body and is a

prognostic marker of complications of traumatic disease in general, in patients of group II on the background of additional introduction to the algorithm of intensive care ceruloplasmin solution. days probably ($p < 0.05$) decreased compared with group I, 26.1 ± 15.6 mg / l and 96.9 ± 28.7 mg / l, respectively. Subsequently, one week after the injury, the level of PSA in the blood of patients in group II was probably ($p < 0.05$) lower than in groups I and III, which was 22.2 ± 11.7 mg / l, 87.6 ± 32.1 mg / l and $68.8 / 31.2$ mg / l, respectively. On the 9th and 12th days of observation, this trend persisted, which determined the positive effect of exogenously administered ceruloplasmin solution on the state of systemic inflammatory response in patients with combined thoracic trauma under conditions of randomization by severity and type of injury. Thus, on the 9th day of treatment, the level of PSA in the blood of patients in group II was $16.7.3$ mg / l, which was probably ($p < 0.05$) lower than in group I, 76.5 ± 29.1 mg / l, and than in group III, 47.8 ± 17.7 mg / l. at the end of the early period of traumatic illness, on the 12th day of hospital stay, the level of PSA in the blood of patients in group II was 12.0 ± 4.1 mg / l, and also probably ($p < 0.05$) was less than in group I, 52.0 ± 21.4 mg / l, and in group III, 34.8 ± 8.2 mg / l. It should be noted that in group III the mean values of the level of PSA in the blood of the studied patients were almost twice less than in group I, but the large variation in the variation of patients did not allow to reach a statistically significant difference. This indicates a positive effect of a solution of D-fructose-1,6-diphosphate sodium salt of the hydrate on the pathogenesis and consequences of hypoxia of mixed origin in combined thoracic trauma, but the presence of probable differences in the level of PSA in the blood between groups I and II and II and III about the significant role of the process of lipid peroxidation, the catalyst of which is endogenous ceruloplasmin, in the occurrence of hypoxia in victims with thoracic trauma with polytrauma.

In turn, a direct analysis of the content of ceruloplasmin in the blood of the studied patients, starting from the 5th day of treatment, a similar dynamics was determined. Thus, on the 5th day of intensive care, the level of CP in the blood of patients in group II was probably ($p < 0.05$) lower than in group I, 273.3 ± 12.6 mg / l and 332.6 ± 42.0 mg / l, respectively. On the 7th and 9th days of treatment, this trend persisted. On the 12th day of hospital stay, the level of CP in the blood of patients in group I was probably ($p < 0.05$) higher than in groups II and III, 303.4 ± 14.1 mg / l, 260.0 ± 13.5 mg / l and 267.7 ± 12.1 mg / l, respectively. The determined dynamics of ceruloplasmin content in the blood of victims with thoracic trauma with polytrauma indicates the predominance of lipid peroxidation mechanisms in the consequences of traumatic disease.

Thus, the obtained data will suggest the appointment of solutions of ceruloplasmin and D-fructose-1,6-diphosphate sodium salt of hydrate in a single algorithm of intensive care in patients with combined thoracic trauma, which is confirmed by the data on CP and PSA in the blood of the studied patients. the end of the early period of traumatic illness.

Discussion of results. Acute respiratory distress syndrome / acute lung injury syndrome is one of the most severe forms of acute respiratory failure, characterized by rapidly increasing peculiar changes in the lungs, persistent hypoxemia and high mortality [14]. This condition is not considered as a separate nosological form, it is always a complication of other serious injuries or diseases. Today, the vast majority of algorithms for the treatment of this pathogenetic condition is characterized by low efficiency [15], which for modern science is a problem that needs to be addressed quickly.

Currently, the diagnosis and determination of the severity of this complication is based on the use of Berlin criteria, including clinical, radiological and physiological indicators characterizing the presence of bilateral pulmonary edema and the severity of oxygenation disorders [16], but does not take into account the phenomenon of mutual burden. injuries. Therefore, it is important to study the leading mechanisms that affect the prognosis of traumatic disease in general, in order to prosthetize these processes in determining their insufficiency. Given the data obtained during the analysis of the dynamics of PSA and CP in the blood of patients with combined thoracic during 12 days in hospital, we can predict the leading pathogenetic mechanism of acute lung injury is oxidative stress.

Conclusions. 1. In patients with combined thoracic trauma, it is important when planning the patient's management tactics to diagnose the content of PSA and CP in the blood during the entire period of stay in the intensive care unit.

2. The level of CP in the blood of patients with combined thoracic trauma is a highly informative diagnostic marker of the impact of hypoxia of mixed genesis on the course of traumatic disease in general.

3. The leading mechanism for the development of acute lung injury syndrome in patients with combined thoracic trauma is oxidative stress, so the appointment of ceruloplasmin as an adjunct to the standard protocol of intensive care is pathogenetically justified.

Conflict of interest. The authors declare no conflict of interest

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