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MECHANISMS OF HEMOSTASIOLOGICAL REACTIONS AND DYSFUNCTION OF THE VASCULAR WALL ENDOTHELIUM IN PATIENTS WITH ACUTE ACETIC ACID POISONING

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✓ ***Resume***

One of the formidable complications of acetic acid poisoning is prolonged intravascular coagulation syndrome (DIC). Many of the key mechanisms of this syndrome remain unexplored. The functional activity of platelets (Tr) and endothelium was investigated. The activity of Tr was determined by the parameters of their aggregation, the function of the endothelium - by the activity of von Willebrand factor (VWF) and the number of desquamated endothelial cells (DEC). It was found that the greatest changes were observed in patients with severe poisoning and were characterized by Tr hypoaggregation, increased EF activity and an increase in the amount of DHEC.

Key words: acetic acid poisoning, hemostasiology, functional activity of platelets, endothelial function.

МЕХАНИЗМЫ ГЕМОСТАЗИОЛОГИЧЕСКИХ РЕАКЦИЙ, И ДИСФУНКЦИЯ ЭНДОТЕЛИЯ СОСУДИСТОЙ СТЕНКИ У БОЛЬНЫХ С ОСТРЫМ ОТРАВЛЕНИЕМ УКСУСНОЙ КИСЛОТОЙ

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✓ ***Резюме***

Одним из грозных осложнений при отравлении уксусной кислотой является синдром длительного внутрисосудистого свертывания(ДВС-синдром). Многие ключевые механизмы этого синдрома остаются неизученными. Была исследована функциональная активность тромбоцитов (Тр) и эндотелия. Активность Тр определяли по параметрам их агрегации, функцию эндотелия — по активности фактора фон Виллебранда (ФВ) и количеству десквамированных эндотелиоцитов (ДЭЦ). Установлено, что наибольшие изменения отмечались у пациентов с тяжелой степенью отравления и характеризовались гипоагрегацией Тр, повышением активности ФВ и увеличением количества ДЭЦ.

Ключевые слова: отравление уксусной кислотой, гемостазиология, функциональная активность тромбоцитов, функция эндотелия

SIRKA KISLOTASIDAN ZAXARLANGAN BEMORLARDA QON TOMIR DEVORI ENDOTELIYSI DISFUNKSIYASI VA GEMOSTAZIOLOGIK REAKSIYALAR MEXANIZMI

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✓ ***Rezume***

Sirka kislotasi bilan zaharlanishning eng dahshatli asoratlaridan biri uzoq vaqt davomida tomir ichi pıhtılaşma sindromi(DCE sindromi). Ushbu sindromning ko'plab asosiy mexanizmlari o'rganilmagan. Trombotsitlar (tr) va endoteliyning funktsional faoliyati tekshirildi. Tr faoliyati ularning agregatsiyasi parametrlari, endotelial funktsiyasi — von Villebrand (FV) omilining faolligi va desquamated endoteliotsitlar soni (desc) bilan aniqlandi. Jiddiy zaharlanish darajasiga ega bo'lgan bemorlarda eng katta o'zgarishlar qayd etildi va tr ning hipoagregatsiyasi, FV faolligining oshishi va DTS sonining ko'payishi bilan tavsiflanadi.

Kalit so'zlar: asatik kislota zaharlanishi, gemostaziologiya, trombotsitlarning funktsional faoliyati, endotelial funktsiyasi

Relevance

Acute poisoning caused by the intake of acetic acid accounts for about 70% of all poisoning with cauterizing agents [1,2].

The leading pathogenetic factor is the aggravating combination of burns of the digestive tract and intravascular hemolysis [6]. At the same time, disorders of vascular-platelet hemostasis, blood coagulation and fibrinolysis are rapidly manifested, leading to the development of disseminated intravascular coagulation, microcirculation disorders and the formation of multiple organ failure [7]. Many key mechanisms of hemostasiological reactions in acetic acid poisoning remain not fully understood.

The purpose of this study is to study the platelet aggregation ability and the severity of endothelial dysfunction in patients with acute acetic acid poisoning at different times from the moment of poisoning.

Material and methods

43 patients with acetic acid poisoning were examined: 25 patients with moderate and 18 patients with severe poisoning. The age of the victims ranged from 18 to 42 years. The average dose of the taken concentrated 70% acetic acid was 42.5 ± 5.4 ml. The control group consisted of 15 healthy individuals. All patients underwent a study of platelet aggregation ability (Tr), the amount of Tr in peripheral blood was calculated. To assess endothelial function, an indicator of von Willebrand factor (VWF) activity and counting the number of desquamated endothelial cells (DEC) were used.

The aggregation of Tr was investigated using the standard turbidimetric method using a two-channel laser aggregation analyzer Tr "Biola" (model LA230). The degree and rate of spontaneous and ADP-induced aggregation of Tr was assessed. An ADP solution at a concentration of 10 and 2.5 μg / ml was used as an inducer of aggregation. Tp was counted using an automatic blood cell counter.

EF activity was determined by the method of ristocetin-cofactor activity, by the method of fluctuating the light flux using a laser aggregation analyzer Tr "Biola" (model LA230). In the blood plasma, the amount of DEC was determined by the Hladovec method [3]. The studies were carried out on 1; 5 and 10 days from the moment of acetic acid poisoning. Statistical processing was carried out in accordance with the Microsoft Excel methodology.

Result and discussion

When analyzing the indices of spontaneous and ADP-induced aggregation Tp, the most pronounced changes were recorded according to the curve of the average size of aggregates. It was found that the lowest aggregation capacity of Tr was observed on the first day after poisoning in patients with moderate and severe poisoning (Table 1). On the 5th day, the degree of aggregation with the addition of high doses of ADP in patients with moderate and severe poisoning was different and amounted to 6.0 = 0.4 and 3.8 = 0.6 relative units. respectively ($p < 0.01$). This indicator was significantly reduced in both groups in comparison with the control (8.9 = 0.5 relative units; $p < 0.001$).

The indicators of the rate of aggregation in these groups had similar changes. Similar differences were obtained with the introduction of small doses of ADP. On day 10, the indicators of aggregation improved in both clinical groups, however, with a severe degree of poisoning, signs of Tr hypoaggregation persisted. Thus, the degree of aggregation was reduced in comparison with the control and amounted to 6.9 ± 0.8 relative units. ($p < 0.05$).

It was found that in patients with severe poisoning, the number of Tr (130 ± 12.5x10 '/ l and 190.6 ± 20, 3x10' / l, respectively) decreased by 1 and 5 trial, and by 10 days their number was restored to normal level. In the group of patients with moderate poisoning, the amount of Tr remained within the normal range throughout the observation period.

In patients with severe poisoning on day 1, the activity of EF increased almost 2 times (205.8 = 17.6%) in comparison with the indicators of healthy people.

Table 1

Change in the aggregation function of platelets for 1 day after poisoning with acetic acid

Severity	Average aggregate size curve					
	Spontaneous aggregation		ADP 10 μg / ml		ADP 2.5 μg / ml	
	Max. meaning	max slope	max, value	max slope	max, value	max slope
Control (M ± t)	1,1±0,1	0,5±0,1	8,9±0,5	27,9±1,5	9,4±0.6	28,2±2,6
Average degree (M ± t)	1,0±0,1 p<0,05	0,5±0,1	6,8±O,6 p <0,05 p,<0,001	18,4±1.5 p <0,001 p <0,001	6,5±0,5 p <0,001 p,<0,001	17,1±1,9 p <0,001 p,<0,001
Severe degree (M ± m)	0,7±0,1 p,<0,001 p,<0,05	0,4±0,1	2,4±0,3 p,<0,001 p <0,001	3,5±O,7 p,<0,001 p <0,001	2,5±0,5 p <0,001 p,<0,001	3,9±1,2 p <0,001 p, <0,001

Notes. p (- reliability of differences in relation to control, p, - reliability of differences between clinical groups.

Normally, the activity of VWF is 50-150%; p <0.01. High PV activity in this group persisted throughout the entire observation period. Among patients with moderate poisoning, the activity of EF tended to increase, but this indicator did not go beyond the upper limit of the norm. It was found that in patients with acetic acid poisoning, the content of DHEC in the peripheral blood increases. The largest number of them was registered in 1 day of poisoning (Table 2).

Thus, the results obtained indicate a decrease in the aggregation function of Tr in patients with acetic acid poisoning. We believe that these changes are possibly secondary and are associated with tissue damage, irritation of the vascular wall by tissue breakdown products and the production of pro-inflammatory cytokines (for example, IL-1, IL-8, TNFa), resulting in activation all links of the hemostasis system. Secondary hypoaggregation of platelets is preceded by their primary hyperaggregation caused by ADP, adrenaline, thrombin, PAF, increased secretion of VWF, inhibition of the formation of prostacyclin, nitric monoxide by endothelial cells [2,3]. Hypoaggregation of platelets against the background of thrombocytopenia is an integral sign of the developed toxic coagulopathy of consumption in patients. This process is facilitated by the appearance in the blood of free hemoglobin, formed as a result of hemolysis of erythrocytes, which leads to accelerated destruction of Tr and aggravation of thrombocytopenia [5].

The content of endothelial cells (X104 / L) in patients with acetic acid poisoning at different times from the moment of poisoning

Table 2

The content of endothelial cells (X104 / L) in patients with acetic acid poisoning at different times from the moment of poisoning

Severity	1 day	5 day	10 day
Control (M ± m)	2,2±0,2	2,2±0,2	2,2±0,2
Average degree (M ± m)	3,2±0,3 p <0,01 p,<0,001	2,6±0,2 p_2<0,001	2,5±0,3
Severe degree (M ± m)	6,6±0,5 p <0,001 p,<0,001	5,6±0,4 p <0,001 p,<0,001	2.9±0,3 p <0,05

Notes p - reliability of differences in relation to control; p, is the reliability of differences between clinical groups.

Acetic acid poisoning is accompanied by changes in the functional state of the endothelium, which can be explained by the activation and damage of endothelial cells. The evidence of endothelial damage is an increase in the content of DHEC in the peripheral blood and an increase in VWF activity. An increase in the amount of DEC can be caused not only by the direct toxic effect of acetic acid on the vascular wall, but also by the influence of proinflammatory cytokines, in particular TNFα, capable of inducing apoptosis of endothelial cells [4,6]. Therefore, desquamated cells, apparently, can be regarded as apoptotic bodies, reflecting the degree of damage to the vascular wall. Endotheliocytes that have undergone apoptosis and entered the circulation have proadhesive and procoagulant properties, promote the development of thrombosis and inflammation [6], which ultimately leads to the formation of multiple organ failure.

The data of this study suggest that the level of decrease in Tr aggregation and an increase in the activity of markers of endothelial damage can objectively reflect the severity of acetic acid poisoning.

Conclusions

1. In patients with acute acetic acid poisoning, significant changes in the aggregation function of platelets were revealed, the severity of which depends on the severity of the poisoning.

2. The aggregation function of platelets in patients with acetic acid poisoning decreases, regardless of their number in the peripheral blood.

3. In patients with acute acetic acid poisoning, endothelial dysfunction was revealed, the severity of which depends on the severity of the poisoning.

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