



STUDY OF SOME INDICES OF KALLIKREIN-KININ SYSTEM AND OF ANGIOTENSIN-CONVERTING ENZYME (KININASE II) IN PLASMA OF RATS ON HEMOPERFUSION WITH NON-ION-EXCHANGE RESIN

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The interest in sorption methods of blood purification rises uninterruptedly. After hemoperfusion (HP) introduction by H. Yatzidis (1964) up to now numerous sorbents have been tested. Activated charcoal is the most frequently used sorbent at present. The first and most important requirement for a given sorbent is to correct disturbed homeostasis during disintoxication by means of prevention of homeostasis disorders. That is why it is necessary to clarify the following interrelations with its application:

1. Sorbent and substances ensuring cell functions: glucose, protein, fats, etc.
2. Sorbent and factors ensuring cell activity: osmotic pressure, temperature, hydrogen ion concentration — pH.
3. Sorbent and substances maintaining the balance of the systems: kallikrein-kinin system (KKS), renin-angiotensin aldosterone system (RAAS).

In the present work we decided to assess the influence of non-ion-exchange resin Wofatit Y-70 (GDR) on the level of some indices responsible for homeostasis maintenance in experimental HP: prekallikrein, slow and rapid kallikrein inhibitors (SIK and RIK, respectively), total proteolytic activity, osmolality, angiotensin-converting enzyme (ACE).

Material and methods

The study was carried out on 35 normal white rats, «Wistar» breed, with 200—300 g b. w. Experimental animals were divided into three groups:

1st — control group — with extracorporeal blood processing, without HP — 19;

2nd group — on HP with uncovered Wofatit Y-70—8;

3rd group — on HP with Wofatit Y-70 covered with human albumin — 8 animals.

HP was performed by using of perfuser — our construction. 8 g sorbent Wofatit Y-70 was applied. The whole system was sterilized by means of Sporotal and washed up with saline. Prior to HP the system was heparinized. HP was realized by using of the peristaltic pump «Haemoflow» (Poland) with output of 1.5 ml/min. During the experiment the animals underwent an inhalation ether narcosis. The vascular approach was performed by cannulation of v. jugularis dextra and a. carotis sinistra by means of teflon catheter. Blood samples with added heparin were taken from the venous end of the system 15 min after HP.

In any groups examined the following plasma parameters were ascertained: KKS indices — prekallikrein, total proteolytic activity, SIK, RIK (1); osmola-

lity (by osmosometer «Knauer»); ACE (3, 4). Results were processed according to the method of variation analysis and then compared by using of t-criterion of Fischer's test.

Results and discussion

The changes of KKS parameters were demonstrated on table 1. It was proved that HP with uncovered Wofatit Y-70 did not cause any statistically significant changes of prekallikrein level. Its reduction was evident only as a tendency. However, prekallikrein decreased statistically reliably ($p < 0.05$) when HP with covered Wofatit Y-70 was applied as compared with its control levels.

Table 1

Changes of some plasma KKS indexes in the three animal groups

Indexes	I st U/l	II nd U/l	III rd U/l
Prekallikrein	128.7 ± 11.7 n=7	104.4 ± 8.3 n=7	86.1 ± 3.3 n=8
Total proteolytic activity	53.4 ± 6.4 n=7	56.6 ± 5.4 n=8	43.9 ± 6.0 n=8
RIK	9.1 ± 2.4 n=7	5.5 ± 1.7 n=7	5.4 ± 0.7 n=8
SIK	1.6 ± 0.3 n=7	1.1 ± 0.2 n=8	1.0 ± 0.1 n=8
	1	2	3

$p^* < 0.05$

3 to 1

Prekallikrein, termed Fletcher's factor, presents a component of importance for Hagemann's factor activation. It is considered that its reduction can be result of its destroyed synthesis in the liver or of its consumption after limiting proteolysis which leads to its transformation into kallikrein. That is why one can judge by prekallikrein decrease of kallikrein increase. The latter can induce an enhanced bradykinin secretion as well as Hagemann's factor activation with consequences on coagulation and transformation of plasminogen into plasmin. Antiproteolytic proteins — alpha₂-macroglobulin, alpha₁-antitrypsin, C₁-inactivator and antithrombin 3rd, divided in the literature into two groups — SIK and RIK — control strictly this system of enzyme reactions (2,5). Our experimental results do not show any statistically significant changes of both inhibitors. When HP with uncovered and covered with albumin Wofatit Y-70 was applied there was a tendency towards inhibitor consumption probably due to controlled proteolysis. It was also confirmed by the fact that total proteolytic activity did not vary significantly from the control values. At this phase of investigation it was difficult to decide if inhibitor synthesis in the liver was increased as a compensatory reaction, or inhibitory capacity was enough to bind with non-functionally liberated proteases.

According to A. H. Nielsen et al. (6), plasma ACE changes could be used as a new method for estimation of the biological compatibility of materials applied in extracorporeal circulation devices. ACE plays a key-role in the mechanisms

T a b l e 2

Changes of plasma ACE in the three animal groups

I st U/l	II nd U/l	III rd U/l
24.25±5.56 n=19	11.63±2.97* n=7	15.08±2.14** n=7
1	2	3
p* < 0.05 p** < 0.05	2 to 1 3 to 1	

regulating blood pressure realizing RAAS—KKS connection. HP on Wofatit Y-70 reduces sharply the enzyme activity (table 2) which is statistically significant ($p < 0.05$). This reduction is 52 per cent for uncovered Wofatit Y-70 but 38 per cent for covered with albumin one.

A tendency is established towards plasma enzyme level enhancement in case of albumin-covered Wofalit Y-70 as compared with that of HP treatment with uncovered Wofatit Y-70. However, there is no significant difference in ACE levels in both animal groups on HP. Sorption of some factors — e. g. of microelements (zinc, etc.) can be discussed as a possible reason for the rather manifested ACE activity diminution in HP. Probably, other components related to the native enzyme state can be absorbed, too. Sharp ACE reduction resulted of HP can possess a clinical importance as far as hypotensive reactions during HP can be expected. ACE changes correlate significantly with prekallikrein ones in the group of HP with covered with albumin Wofatit Y-70 ($r = -0.65$).

The investigation of osmolality demonstrates that in all groups of experimental animals there are no statistically significant differences (table 3). Nevertheless, the course of osmolality changes follows the direction of ACE ones without any correlation between these two parameters.

T a b l e 3

Osmolality changes in the three animal groups

I st mOsm/kg	II nd mOsm/kg	III rd mOsm/kg
326.61±4.53 n=9	317.58±13.86 n=6	324.63±4.81 n=8

Our results concerning the changes of the parameters of KKS, ACE, and osmolality (table 1, 2, 3) show that there is a tendency towards a relatively better compatibility when albumin-covered Wofatit Y-70 is applied.

We can draw the following conclusions:

1. KKS parameters (SIK, RIK, total proteolytic activity) do not change statistically significantly in HP with Wofatit Y-70. It is proved that prekallikrein diminishes statistically significantly after HP with albumin-covered Wofatit Y-70.

2. HP induces a significant ACE activity decrease which is less manifested when albumin-covered Wofatit Y-70 was applied.

3. No statistically considerable changes of osmolality level are ascertained after HP treatment.

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ИССЛЕДОВАНИЕ НЕКОТОРЫХ ПОКАЗАТЕЛЕЙ КАЛЛИКРЕИН-КИНИНОВОЙ СИСТЕМЫ И АНГИОТЕНЗИН-ПРЕВРАЩАЮЩЕГО ЭНЗИМА (КИНИНАЗА II) В ПЛАЗМЕ КРЫС С ПРИМЕНЕНИЕМ ГЕМОПЕРФУЗИИ НЕЙНООБМЕННОЙ СМОЛЫ

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РЕЗЮМЕ

Исследовано влияние нейнообменной смолы Wofatit Y-70 — ГДР на уровень некоторых показателей калликреин-кининовой и ренин-ангиотензин-альдостероновой систем у крыс с применением экспериментальной гемоперфузии.

Эксперимент был проведен на 35 здоровых крысах-самцах линии «Wistar», распределенных в три группы: I группа — контрольная, с экстракорпоральной обработкой крови без гемоперфузии; II группа — с применением гемоперфузии с помощью Wofatit Y-70 без покрытия; III группа — с применением гемоперфузии при использовании Wofatit Y-70, покрытого гуманальбумином.

Показатели калликреин-кининовой системы — быстро (быстрый ингибитор калликреина) и медленно (медленный ингибитор калликреина) действующие ингибиторы, а также общая протеолитическая активность не показывают статистически значимых изменений при гемоперфузии с использованием Wofatit Y-70. Доказано статистически значимое уменьшение прекалликреина после гемоперфузии с использованием покрытого альбумином Wofatit Y-70. Гемоперфузия приводит к статистически значимому понижению активности ангиотензин-превращающего энзима, что при исследовании покрытого альбумином Wofatit Y-70, показало более слабую выраженность. Для исследования осмолальности после гемоперфузии статистически значимых изменений не устанавливается.