**THE ROLE OF INTESTINAL TRANSLOCATION IN THE ORIGIN OF ENDOTOXEMIA IN ACUTE POISONING AND DETOXIFICATION EFFECT OF INTESTINAL LAVAGE**

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**BAKGROUND** Endogenous intoxication (EI), following acute poisoning, aggravates the disease course, increases the risk of complications and death, as well as the scope and duration of therapeutic measures. That is why, prevention and correction of EI in acute poisoning with psychopharmacological drugs (PPD) as well is relevant.

**MATERIAL AND METHODS** In 115 patients with PPD poisoning, intestinal lavage (IL) was performed, 50 patients were control group.

EI was evaluated by the level of medium molecular weight peptides (MMWP) and lipopolysaccharides (LS) in serum, albumin tests, leukocyte index of intoxication (LII) and shear index of neutrophils (SIN). The level of MMWP in blood and intestinal lavage fluid (intestinate) in 23 patients and

22 healthy donors was measured.

**RESULTS** Initial level of WWMP in the blood of patients exceeded the norm by 32%, LS — by 10 times, LII — by

6.3 times and SIN — by 2.4 times. At the beginning of the gastrointestinal lavage, the intestinate’s

MMWP in patients and donors exceed their values in the blood. At the end of the IL it fell by 3–

6 times. This was accompanied by a fall of MMWP in blood of patients by 18.2%, LS — 50%, and LII

and SIN by 52% and 70% respectively. In the comparison group LII and SIN continued to grow during

the 1st day.

**CONCLUSION** In patients with uncomplicated poisoning with PPD the source of endotoxemia was the intestines.

The IL promotes the elimination of endogenous toxins and the reduction of EI.

**Keywords:** acute poisoning, endogenous intoxication, intestinal lavage.

aRAB – reserve albumin binding (absolute)

DR – distribution ratio

ECA – effective concentration of albumin

EI – endogenous intoxication
EIR – endogenous intoxication ratio

IL – intestinal lavage

LII – leukocyte index of intoxication

LS – lipopolysaccharide

MMWP – medium molecular weight peptide

PPD – psychopharmacological drug

SIN – shear index of neutrophils

sRAB – reserve albumin binding (specific)

TCA – total concentration of albumin
TI – toxicity index

INTRODUCTION

The development of endogenous intoxication (EI) begins already at a toxicogenic stage, and its manifestation is fully observed at a somatogenic stage of sharp poisoning, especially in the presence of complications [1, 2]. EI develops as a result of a pathological metabolism with formation and accumulation of toxic substances of an endogenous origin in organs and tissues, and also with increase of their amount in blood [3]. Severity of EI correlates with the endotoxemia level, which may be eliminated with a complex of sorption and dialysis and filtration methods of detoxification, physical and chemical hemotherapy and an enterosorption [4–7].

According to a number of authors, one of pathogenic mechanisms of endotoxemia in critical conditions of various etiology is the increase in a stream of toxic substances from intestines due to the growth of intestinal barrier permeability and strengthening of virulence and invasiveness of opportunistic intestinal flora [8, 9]. When intestinal microbial toxins (including lipopolysaccharides (LPSs) initiating system inflammatory reaction) enter the internal environment they may cause infectious complications and polyorganic insufficiency [8]. There are single papers saying that the syndrome of the increased permeability of an intestinal wall with intensive intake of endogenous toxicants in blood also develops in acute poisonings with barbiturates and the cauterizing substances [10-12]. However, in the literature there are no options of therapy for pathological intestinal translocation of endogenous toxicants into the internal environment of an organism.

Research objective: to estimate a role of endogenous toxicants translocation in pathogenesis of EI through the example of PPDs poisoning and effect of IL.

MATERIAL AND METHODS

We studied 187 patients aged 18-65 years: 57.5% women and 42.5% men. The total number of observed patients was 165. These patients had serious multi-poisoning with PPDs. In 115 patients, IL was included into treatment, and in 50 patients who were the comparison group, blood detoxification methods (hemosorption and hemodialysis), traditional laxatives and pharmacological stimulation of intestines were used. The serious poisoning with PPDs manifested with depressed consciousness down to a deep coma (score 3–5, the Glasgow Coma Scale).

The EI was assessed according to the level of medium molecular weight peptides (MMWPs) in serum of blood [13], the effective concentration of albumin (ECA), the total concentration of albumin (TCA) [14], calculated rates of specific and absolute reserve binding capacity of albumin (sRBA, aRBA), and also the toxicity index (TI) [14, 15].

The specific RBA was calculated using the formula:

sRBA (%) = ECA (g/l)/TCA (g/l) x100%.

According to authors, this indicator reflects the specific weight of the sorption centers of albumin in serum which aren't blocked by toxicants [14].

aRBA was calculated using the formula:

aRSA (g/l) = TCA (g/l) — ECA (g/l),

which corresponds to concentration of the albumin blocked by toxicants [15].

According to N. M. Fedorovsky [15], TI is the universal integrated indicator reflecting the extent of the albumin sorption centers blockade with a toxicant which is calculated using the formula:

TI = (TCA/ECA) – 1.

The distribution ratio was also calculated [16, 17]:

DR = MMWPs280/MMWPs254

and endogenous intoxication ratio (EIR) [18, 19]:

EIR = (MMWPs254/ECA) ×1000).

The EI was also assessed according to hematologic indexes — leukocyte index of intoxication (LII) and the shear index of neutrophils (SIN) [20].

We measured LSs in blood serum using the modified technique of N.V. Yevdokimova et al. to confirm translocation of intestinal microbe toxins in PPDs poisonings in 23 patients [21].

We have considered necessary to study normal and pathologic regularity of endogenous toxicants distribution between an intestinal lumen and blood for specification of endotoxemia development, reasonability and effectiveness of IL. We observed 22 almost healthy donors and 23 patients with uncomplicated poisoning with PPDs with revealed MMWPs in intestinal washings and blood in the beginning and in the end of the IL.

Patients with PPDs poisonings underwent IL within 5 hours after the admission. The saline enteral solution (isoionicto chymus and isoosotic to plasma) was administered through a naso-gastric or naso-jejunal probe. Donors drank 4 l of the solution by 150 ml portions every 5 min. Diarrhea developed after introduction of 1.5-2.5 l of solution. Intestines had been lavaged for 3–6 hours until the intestinal content became clean [22].

RESULTS AND DISCUSSION

 Distribution of MMPs in washings of intestines and blood of volunteers and patients with PPDs poisonings is presented on fig. 1.

Словосочетания



Fig. 1. The comparative characteristic of medium molecular weight peptides (E254) content in blood and the first portion of intestinal washings in almost healthy people (A) and patients with the multi PPDs poisoning (B)

Note: \* — statistically significant difference from a blood indicator (р<0.05, the Student’s t-criterion)

On fig. 1, it is visible that donors had a normal MMWPs level, and in patients with PPDs poisoning it exceeded the normal level by 32% (E254 fraction). In the first liquid portion of intestinal washings of volunteers and patients with PPDs poisonings the concentration of MMWPs exceeded its concentration in blood by 4.7 and 3.4 times, respectively. By the end of IL, concentration of MMWPs in volunteers in the last portion of intestinal washings fell by 6 times, and in patients with poisonings — by 3.3 times (fig. 2). After the IL, the concentration of MMWPs in intestinal washings compared to blood both in volunteers and patients became consistent.



Fig. 2. Changes of MMWPs (E254) concentration in intestinal washings of almost healthy volunteers (A) and patients with the combined poisoning with psychopharmacological drugs (B) at the beginning and the end of an intestinal lavage

Note: \* — statistically significant variation from an indicator of an initial portion of intestinal washings (р<0.05, the Student’s t-criterion)

Thus, in the course of IL there was elimination of MMWPs from intestines followed by positive changes of IL indicators at PPDs poisoning presented in tab. 1.

Table 1

Influence of an intestinal lavage on indicators of endogenous intoxication under the multi-poisoning with psychopharmacological drugs, n=115

|  |  |  |
| --- | --- | --- |
| Blood parameters | Normal | Stages of the study |
| Before IL | ∆, %1 | After IL | ∆, %2 | After 3 days | ∆, %2 |
| MMWPs *Е254* | 0.200±0.003 | 0.264±0.018 | 32 | 0.216±0.0122 | – 18.2 | 0.219±0.012 | – 17 |
| MMWPs *Е280* | 0.275±0.003 | 0.33±0.029 | 20 | 0.272±0.0282 | – 17.6 | 0.285±0.025 | – 13.6 |
| DR, units | 1.3±0.36 | 1.25±0.3 | – 3.8 | 1.26±0.06 | 0.8 | 1.3±0.04 | 4 |
| EIR, units | 4.9±1.38 | 9.635±0.31 | 96.6 | 6.0±0.052 | – 37.5 | 7.5±0.05 | – 22.16 |
| TCA, g/l  | 47.8±0.73 | 39.13±1.81 | – 18.1 | 37.6±1.5 | – 3.9 | 31.4±3.02 | – 19.7 |
| ECA, g/l | 40.7±2.18 | 27.4±2.71 | – 32.7 | 35.9±1.72 | 31 | 29.0±1.6 | 5.8 |
| sRAB, % | 84.0±5.1 | 70.5±7.2 | – 16.1 | 95.9±8.72 | 36.0 | 92.1±4.02 | 30.6 |
| aRAB, g/l | 7.1±1.45 | 11.95±1.71 | 68.3 | 1.8±0.42 | – 84.9 | 2.7±0.52 | – 77.4 |
| TI, units | 0.17±0.01 | 0.45±0.041 | 164.7 | 0.05±0.022 | – 88.9 | 0.09±0.032 | – 80.0 |

Note: 1 — statistically significant variation from a normal value 2 — statistically significant variation from an initial indicator (р<0.05, the Student’s t-criterion); ∆, %1 — compared to a normal value; ∆, %2 — compared to an initial value. IT — index of toxity; IL — intestinal lavage; DR — distribution ratio; EIR — endogenous intoxication ratio; TCA — total concentration of albumin; aRAB – reserve albumin binding (absolute), sRAB – reserve albumin binding (specific); MMWPs – medium molecular weight peptides; ECA — effective concentration of albumin

 After the IL in group of patients with a PPDs poisoning we noted a fall of MMWPs fractions in blood by 1.2 times, EIR — by 1.6 times, 31% rise of ECA in blood for 31% with increase in specific weight of the free centers (sRBA) by 1,4 times, reduction of a pool of the blocked sorption centers of albumin (aRBA) by 6.6 times, and also decrease in IT by 9 times in relation to an initial state that in general reflected considerable fall of endotoxemia.

Before the IL, the LS level in blood of patients with a serious PPDs poisoning exceeded the normal parameter by more than 10 times (fig. 3). After the IL, we noted reduction of this indicator by 1.8 times which decreased twice within the next days (р<0.05). The findings showed that washing of intestines promoted the fall of LS concentration in blood of patients with PPDs poisoning, but one session of IL appeared to be insufficient as in the recurrence of gradual LS increase took place within the subsequent period (up to 7 days)



Fig. 3. Changes of lipopolysaccharides concentration in blood of patients with the multi-poisoning with psychopharmacological drugs before and after the intestinal lavage (n=23)

Note: \* — statistically significant variation from an initial indicator (р<0.01 according to Wilcoxon test); \*\* — norm to 0.06 EU/ml. IL — intestinal lavage; LPSs — lipopolysaccharides

Results of studying of influence of IL on hematologic indexes of intoxication in patients with a serious PPDs poisoning are shown in tab. 2.

The tab. 2 demonstrates that the LII and SIN initial levels exceeded normal levels by 6.3 and 2.4 times, respectively. After the IL, there was an improvement of integrated indicators of intoxication (fall of LII and SIN of more than for 52% and 70%, respectively) that also demonstrated reduction of EI severity.

Table 2

Changes of integrated indicators of intoxication associated with IL in patients with a serious PPDs poisoning, n=102

|  |  |  |
| --- | --- | --- |
| EI parameters | NNormal | Values before and after IL |
| Before IL | ∆, %1 | After IL | ∆, %2 |
| LII | 1.0±0.5 | 6.3±0.71 | 530 | 3±0.62 | – 52.4 |
| SIN | 0.06±0.02 | 0.143±0.031 | 138 | 0.042±0.0092 | – 70.6 |

Note: 1 — statistically significant variation of an initial parameter from a normal value, 2 — statistically significant variation from an initial parameter (р<0.05, the Student’s t-criterion); ∆, %1 — compared to a normal value; ∆, %2 — compared to an initial value. SIN — shear index of neutrophils; IL — intestinal lavage; LII — leucocytes index of intoxication

Changes of integrated indicators of intoxication in the comparison group with a serious PPDs poisoning are shown in tab. 3.

Table 3

Changes of integrated indicators of intoxication at stages of examination of the comparison group patients with the serious multi-poisoning with psychopharmacological drugs, n=50

|  |  |
| --- | --- |
|  | Parameters |
| LII (*N*=1.0±0.5) | Δ, % | SIN (*N*=0.06±0.02) | Δ, % |
| Initial | 6.1±1.11 | 510 | 0.13±0.041 | 117 |
| After 24 hours | 7.4±1.6 | 640 | 0.18±0.05 | 200 |
| After 36 hours | 5.2±0.8 | 420 | 0.17±0.07 | 183.3 |
| After 120 hours | 3.5±0.42 | 250 | 0.12±0.03 | 100 |

Note: 1 — statistically significant variation of an initial parameter from a normal value, 2 — statistically significant variation from an initial parameter (р<0.05, the Student’s t-criterion); ∆, %— compared to a normal value; SIN — shear index of neutrophils; LII — leucocytes index of intoxication

Apparently from tab. 3, the initial value of LII in the group exceeded the normal value by 6 times. Within the next days this indicator continued to grow. Only on day 3 there was a tendency to its decrease, and on day 5 it became 1.7 times lower in relation to an initial value with statistically significant distinction of indicators (р<0.05). The initial value of SIN in the comparison group exceeded a normal value more than twice. This indicator increased by 3 times in 24 hours, and then it began to fall and approached initial values on day 5.

Thus, in serious PPDs poisonings initially high values of integrated indicators of intoxication significantly decreased by the time of the IL termination while under the standard methods of treatment similar changes were noted only by day 5.

The report has shown that human intestines contain a significant amount of endogenous toxicants, which agrees with A.L. Kostyuchenko's et al. statement [23]. In washing waters of intestines of both donors and patients with PPDs poisoning the concentration of MMWPs was many times higher, than in blood. At the same time, some distinction in the ratio *MMWPs in intestinal washings/MMWPs in blood* of volunteers (4.7:1) and patients with poisonings attracted attention (3.4:1). It was caused by the fact that in patients with PPDs poisonings the concentration of MMWPs in blood was higher, than in volunteers, but it was lower in the intestinal washings. Such variation can be explained with redistribution of MMWPs between intestines and blood against the increased permeability of an intestinal barrier in patients with poisonings. It is known, that permeability of an intestinal epithelium for substances of average and big molecular weight increases under GI-tract paresis, violation of the acid-base state and hydro-electrolytic balance of blood, microcirculation with non-ooccluding heart attacks in an intestinal mucous membrane, changes of the quantitative and qualitative characteristics of a microbiocenosis of intestines followed by a decrease in colonial resistance of mucous flora, local immunity, etc. [8, 24, 25]. The mentioned disorders occur in a serious poisoning with PPDs [26, 27]. In healthy faces, the bulk of endogenous toxicants under the normal permeability of an intestinal barrier concentrates in a lumen of intestines and is removed naturally.

CONCLUSION

Thus, in uncomplicated poisonings with PPDs when there are no inflammation foci and destruction of tissues, the increased concentration of MMWPs and LSs in blood having "an intestinal origin" points that the main source of endotoxemia are intestines under condition that the entero-humoral barrier fails (pre-and epithelial barriers of an intestinal wall, immune system of portal vein system, hepatic and pulmonary macrophages).

The intestinal lavage decreases the pool of endogenous toxicants in intestines and thereby reduce its enter to the inner environment even under the increased permeability of an entero-humoral barrier, that is confirmed by a decrease in level of endotoxemia and endogenous intoxication.

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