

# Indices of Hepatocellular Function at Extracorporeal Detoxification in Patients with Obstructive Jaundice Complicated by Liver Failure

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**Abstract** Aim of study was to improve the surgical treatment results of patients with endogenous intoxication and hepatocellular insufficiency on the background of obstructive jaundice by developing an original method of extracorporeal detoxification. **Material and methods.** The authors evaluated the effectiveness of the improved method of hyperbaric plasma adsorption in the treatment of severe obstructive jaundice. 50 patients treated in the clinic of the Andijan State Medical Institute in 2018-2019 were selected for the study. The study included only patients with severe obstructive jaundice on the background of cholelithiasis complicated by choledocholithiasis. Sessions of modified plasma adsorption were conducted in patients with obstructive jaundice and liver failure. **Conclusion.** The use of the improved technique of hyperbaric plasma adsorption in the complex treatment of the complicated course of obstructive jaundice by the third day after the choledocholithiasis allowed to accelerate the regression of hyperbilirubinemia from  $201.5 \pm 19.0$  to  $75.4 \pm 11.3$   $\mu\text{mol} / \text{L}$ . These indices decreased from  $194.3 \pm 13.2$  to  $131.5 \pm 13.1$   $\mu\text{mol} / \text{L}$  ( $t = 3.24$ ;  $p < 0.05$ ) at standard conservative therapy. Accordingly, we observed a more intense decrease in the severity of the patients' condition (from  $11.1 \pm 1.3$  to  $3.5 \pm 1.0$  points versus - from  $11.1 \pm 0.9$  to  $7.4 \pm 1.0$  points;  $t = 2.75$ ;  $p < 0.05$ ). Indicators of hemostasis and inflammation markers were also significantly improved 3-5 days after procedures.

**Keywords** Choledocholithiasis, Obstructive jaundice, Liver failure, Plasma adsorption

## 1. Introduction

According to the World Health Organization, biliary tract diseases affect a significant part of the world's population. One of the most common complications of this disease is obstructive jaundice which makes up approximately 45-50% of cases among all types of jaundice [1]. The highest rates of cholelithiasis are recorded in Western countries - 64% for women and 29% for men. The Asian region has an intermediate prevalence of 13.9% for women and 5.3% for men. However, the available statistics show that the prevalence of liver failure associated with obstructive jaundice is the highest among the population of the Asian continent [2]. New research in hepatology has significantly improved the understanding of the processes occurring at obstructive jaundice for recent years. Despite the presence of a large number of reasons that cause obstruction of the biliary tract, the mechanisms of the pathogenesis of the development of hepatic failure are non-specific and the main features of these changes for various etiological reasons are the same [3]. In most clinical

situations associated with obstructive jaundice, one has to deal with endogenous intoxication, which is a sophisticated pathogenetic complex, including metabolic and functional disorders of almost all organs and systems. Today, ways to improve the results of obstructive jaundice treatment have the goal of not only improving the technical means of surgical treatment, but also eliminating the main causes of complications and mortality (cholemic and inflammatory intoxication). The methods of efferent therapy have been increasingly used to achieve this goal for recent decades. Many studies have been published on the use of extracorporeal hemocorrection methods in the treatment of liver failure, both acute and chronic for the past 20 years. The literature data are contradictory, based on the analysis of treatment results of small and heterogeneous groups of patients [4-5]. There are no studies that evaluate the complex application of various extracorporeal detoxification methods in the available literature. Most hepatology clinics in our country adhere to conservative treatment tactics for patients. There are disagreements in the definition of treatment tactics for severe liver lesions, especially in the fulminant variant of the course of the disease. There is still no consensus on the effectiveness of plasmapheresis in severe liver lesion associated with obstructive jaundice [6-8]. The appearance

of modern hemato-processors and devices for artificial support of the main liver functions, advances in transfusiology and resuscitation, new technologies in liver surgery allow to study the problem of treating liver failure from new positions and at a modern level.

**Aim of study** was to improve the surgical treatment results of patients with endogenous intoxication and hepatocellular insufficiency on the background of obstructive jaundice by developing an original method of extracorporeal detoxification.

## 2. Material and Methods

The main direction for the clinical stage of research was the assessment of the improved method of hyperbaric plasma adsorption effectiveness in the treatment of severe obstructive jaundice. 50 patients treated in the clinic of the Andijan State Medical Institute in 2018-2019 were selected for the study. The study included only patients with severe obstructive jaundice on the background of cholelithiasis complicated by choledocholithiasis. All patients were divided into two groups. The main group included 19 patients treated in 2019, who were used an improved method of hyperbaric plasma sorption in complex treatment after endoscopic or surgical elimination of obstructive jaundice cause (choledocholithiasis). The comparison group included 31 patients treated in 2018, in whose rehabilitation the standard protocol for the management of patients with complicated obstructive jaundice was applied. There were 38 (74%) women and 12 (26%) men. The mean age was 43 years. Endoscopic papillosphincterotomy (EPST) with lithoextraction was performed in 21 cases, suprapapillary choledochoduodenostomy (SPCDS) with lithoextraction - in 8 (16%) patients and cholecystectomy, choledocholithotomy with drainage according to Ker – in 21 (42.0%). All patients according to the severity of obstructive jaundice were distributed according to the classification of E.I. Halperin (2012), proposed to assess and predict postoperative results. Initially, the assessment took into account the indicators of total bilirubin and total protein, but later in 2013 E.I. Halperin presented a simplified classification that takes into account only the total bilirubin indicator. Classification also takes into account the manifestations of complications of obstructive jaundice (cholangitis, renal failure, liver failure (signs of encephalopathy), gastrointestinal bleeding, sepsis). The total bilirubin level is distributed as follows:  $<60 \mu\text{mol} / \text{L}$  - 1 point,  $60-200 \mu\text{mol} / \text{L}$  - 2 points,  $\geq 200 \mu\text{mol} / \text{L}$  - 3 points (Tab. 1).

Any of these complications and the tumor etiology of obstructive jaundice are estimated 2 times higher than the bilirubin score (if total bilirubin - 1 point, then complication is 2 points, if bilirubin - 2 points - complication is 4 points, and if bilirubin 3 points - complication is 6 points). Accordingly, the severity of obstructive jaundice is divided into: mild (class A -  $\leq 4$  points), moderate (class B - 5–13 points) and severe (class C -  $\geq 14$  points) (Tab. 2).

**Table 1.** Distribution of patients by bilirubinemia level (according to E.I. Galperin)

| Total bilirubin level               | Main group |        | Comparison group |        |
|-------------------------------------|------------|--------|------------------|--------|
|                                     | absolute   | %      | absolute         | %      |
| 60-200 $\mu\text{mol} / \text{L}$   | 11         | 57.9%  | 18               | 58.1%  |
| $\geq 200 \mu\text{mol} / \text{L}$ | 8          | 42.1%  | 13               | 41.9%  |
| Total                               | 19         | 100.0% | 31               | 100.0% |

**Table 2.** Distribution of patients according to the severity of obstructive jaundice according to E.I. Galperin

| The severity level of obstructive jaundice | Main group     |                | Comparison group |                |
|--|----------------|----------------|------------------|----------------|
|  | absolute       | %              | absolute         | %              |
| Class B (5-13 points)                      | 11             | 57.9%          | 19               | 61.3%          |
| Class C ( $\geq 14$ points)                | 8              | 42.1%          | 12               | 38.7%          |
| <b>Total</b>                               | <b>19</b>      | <b>100.0 %</b> | <b>31</b>        | <b>100.0 %</b> |
| Mean point ( $M \pm \delta$ )              | 11.1 $\pm$ 5.5 |                | 11.1 $\pm$ 4.9   |                |

The following methods were used to achieve the set objectives: general clinical, laboratory, instrumental, special and statistical research methods.

## 3. Results

Table 3 shows the dynamics of total bilirubin depending on the patient's initial class according to the severity of the obstructive jaundice clinical course. So, according to the baseline indicators of total bilirubin in classes "B" and "C" the compared groups were representative, with a coefficient of representativeness of 1.54.

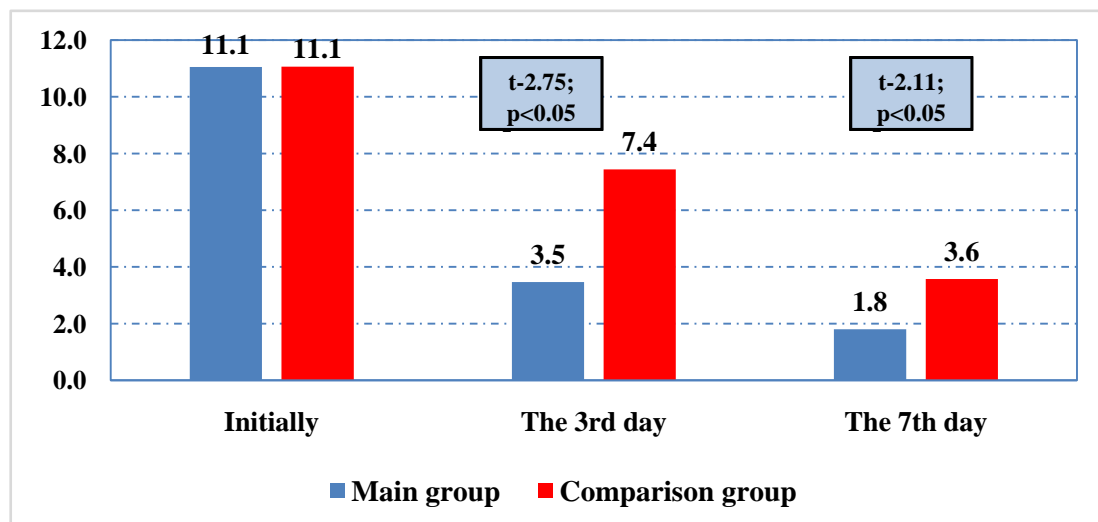
There was a clear tendency for a more significant drop in total bilirubin levels in the main group with functional class "B" after the first day of treatment from  $172.8 \pm 19.3 \mu\text{mol} / \text{L}$  to  $139.6 \pm 18.0 \mu\text{mol} / \text{L}$  and on the 7<sup>th</sup> day to  $39.2 \pm 7.5 \mu\text{mol} / \text{L}$  versus the comparison group. There was a decrease from  $168.9 \pm 15.6 \mu\text{mol} / \text{L}$  to  $152.4 \pm 15.0 \mu\text{mol} / \text{L}$  on the first day, and on the 7<sup>th</sup> day to  $83.8 \pm 12.5 \mu\text{mol} / \text{L}$  (with a significant difference for the first day  $p > 0, 05$  and for the 7<sup>th</sup> day  $p < 0.05$ , while the t-test was determined within -0.16 and 3.06, respectively).

In spite of more severe clinical course of this complication, similar dynamics were observed in patients of the main group with functional class "C". So, after the first day of treatment, total bilirubin decreased from  $240.9 \pm 36.0 \mu\text{mol} / \text{L}$  to  $209.0 \pm 34.0 \mu\text{mol} / \text{L}$  and on the 7<sup>th</sup> day - to  $59.6 \pm 14.5 \mu\text{mol} / \text{L}$ , in contrast to the comparison group, where the result on the first day showed a decrease from  $234.4 \pm 18.7 \mu\text{mol} / \text{L}$  to  $223.3 \pm 21.7 \mu\text{mol} / \text{L}$  and on 7<sup>th</sup> day - to  $93.8 \pm 15.7 \mu\text{mol} / \text{L}$  (with a significant difference for the first day,  $p > 0.05$ ; for 7<sup>th</sup> day,  $p < 0.05$ , while the t-test was determined within -0.30 and 3.25, respectively). It is more preferable for most practicing surgeons, to assess the dynamics of the severity of obstructive jaundice in points according to E.I. Galperin (2012) which is reflected in Table 4 and Fig. 1.

**Table 3.** Dynamics of total bilirubin

| The severity level of obstructive jaundice | Index  | Days      |       |       |       |       |       |
|--|--------|-----------|-------|-------|-------|-------|-------|
|  |        | Initially | 1     | 2     | 3     | 5     | 7     |
| Main group                                 |        |           |       |       |       |       |       |
| Class B (5-13 points)                      | M      | 172.8     | 139.6 | 99.5  | 68.9  | 51.5  | 39.2  |
|  | δ      | 64.1      | 59.7  | 48.6  | 39.2  | 30.7  | 23.8  |
|  | m      | 19.3      | 18.0  | 14.7  | 12.4  | 9.7   | 7.5   |
| Class C (≥14 points)                       | M      | 240.9     | 209.0 | 156.6 | 88.4  | 74.6  | 59.6  |
|  | δ      | 101.8     | 96.3  | 93.1  | 54.1  | 41.0  | 32.4  |
|  | m      | 36.0      | 34.0  | 35.2  | 24.2  | 18.3  | 14.5  |
| All patients                               | M      | 201.5     | 168.8 | 121.7 | 75.4  | 59.2  | 46.0  |
|  | δ      | 86.6      | 82.6  | 72.6  | 43.8  | 34.8  | 27.6  |
|  | m      | 19.9      | 18.9  | 17.1  | 11.3  | 9.0   | 7.1   |
| Comparison group                           |        |           |       |       |       |       |       |
| Class B (5-13 points)                      | M      | 168.9     | 152.4 | 141.3 | 117.4 | 101.4 | 83.8  |
|  | δ      | 68.0      | 65.3  | 65.8  | 62.0  | 58.2  | 49.8  |
|  | m      | 15.6      | 15.0  | 15.1  | 15.0  | 14.6  | 12.5  |
|  | t-test | -0,16     | 0.55  | 1.99  | 2.49  | 2.85  | 3.06  |
|  | P      | >0.05     | >0.05 | >0.05 | <0.05 | <0.05 | <0.05 |
| Class C (≥14 points)                       | M      | 234.4     | 223.3 | 220.6 | 161.4 | 152.1 | 93.8  |
|  | δ      | 64.8      | 75.3  | 89.8  | 66.2  | 84.4  | 35.0  |
|  | m      | 18.7      | 21.7  | 25.9  | 23.4  | 31.9  | 15.7  |
|  | t-test | -0.16     | 0.35  | 1.46  | 2.17  | 2.11  | 1.60  |
|  | P      | >0.05     | >0.05 | >0.05 | <0.05 | <0.05 | >0.05 |
| All patients                               | M      | 194.3     | 179.8 | 172.0 | 131.5 | 116.8 | 86.1  |
|  | δ      | 73.3      | 76.6  | 84.2  | 65.4  | 69.5  | 46.1  |
|  | m      | 13,2      | 13.8  | 15.1  | 13.1  | 14.5  | 10.1  |
|  | t-test | -0.30     | 0.47  | 2.20  | 3.24  | 3.38  | 3.25  |
|  | P      | >0.05     | >005  | <0.05 | <0.05 | <0.05 | <0.05 |

Note: M – mean value; δ – standard deviation; m – mean error of the mean value; t-test and P – significance of confidence between groups

**Figure 1.** The dynamics of the obstructive jaundice severity in points according to E.I. Galperin

**Table 4.** Dynamics of total bilirubin depending on the initial level of bilirubinemia (according to E.I. Galperin)

| Level of bilirubinemia | Index  | Days      |       |       |       |       |       |
|------------------------|--------|-----------|-------|-------|-------|-------|-------|
|                        |        | Initially | 1     | 2     | 3     | 5     | 7     |
| Main group             |        |           |       |       |       |       |       |
| 60-200 μmol / l        | M      | 139.5     | 110.6 | 75.9  | 50.8  | 37.1  | 28.6  |
|                        | δ      | 32.8      | 27.4  | 21.0  | 14.5  | 8.7   | 4.2   |
|                        | m      | 9.9       | 8.3   | 6.3   | 4.6   | 2.8   | 1.3   |
| ≥200 μmol / l          | M      | 286.8     | 248.9 | 193.6 | 124.6 | 103.4 | 80.8  |
|                        | δ      | 58.4      | 61.9  | 65.8  | 41.2  | 20.3  | 19.1  |
|                        | m      | 20.6      | 21.9  | 24.9  | 18.4  | 9.1   | 8.5   |
| Comparison group       |        |           |       |       |       |       |       |
| 60-200 μmol / l        | M      | 140.2     | 126.4 | 116.7 | 93.9  | 81.1  | 59.4  |
|                        | δ      | 31.8      | 34.3  | 40.5  | 37.1  | 43.3  | 20.5  |
|                        | m      | 7.5       | 8.1   | 9.6   | 9.3   | 11.2  | 5.5   |
|                        | t-test | 0.06      | 1.37  | 3.56  | 4.17  | 3.83  | 5.45  |
|                        | P      | >0.05     | >0.05 | <0.05 | <0.05 | <0.05 | <0.05 |
| ≥200 μmol / l          | M      | 269.1     | 253.8 | 248.5 | 198.2 | 183.8 | 139.7 |
|                        | δ      | 39.3      | 53.0  | 67.0  | 49.3  | 59.7  | 33.9  |
|                        | m      | 10.9      | 14.7  | 18.6  | 16.4  | 21.1  | 12.8  |
|                        | t-test | -0.76     | 0.19  | 1.77  | 2.98  | 3.50  | 3.82  |
|                        | P      | >0.05     | >0.05 | >0.05 | <0.05 | <0.05 | <0.05 |

**Table 5.** The dynamics of the patients' condition severity after endoscopic procedure for obstructive jaundice

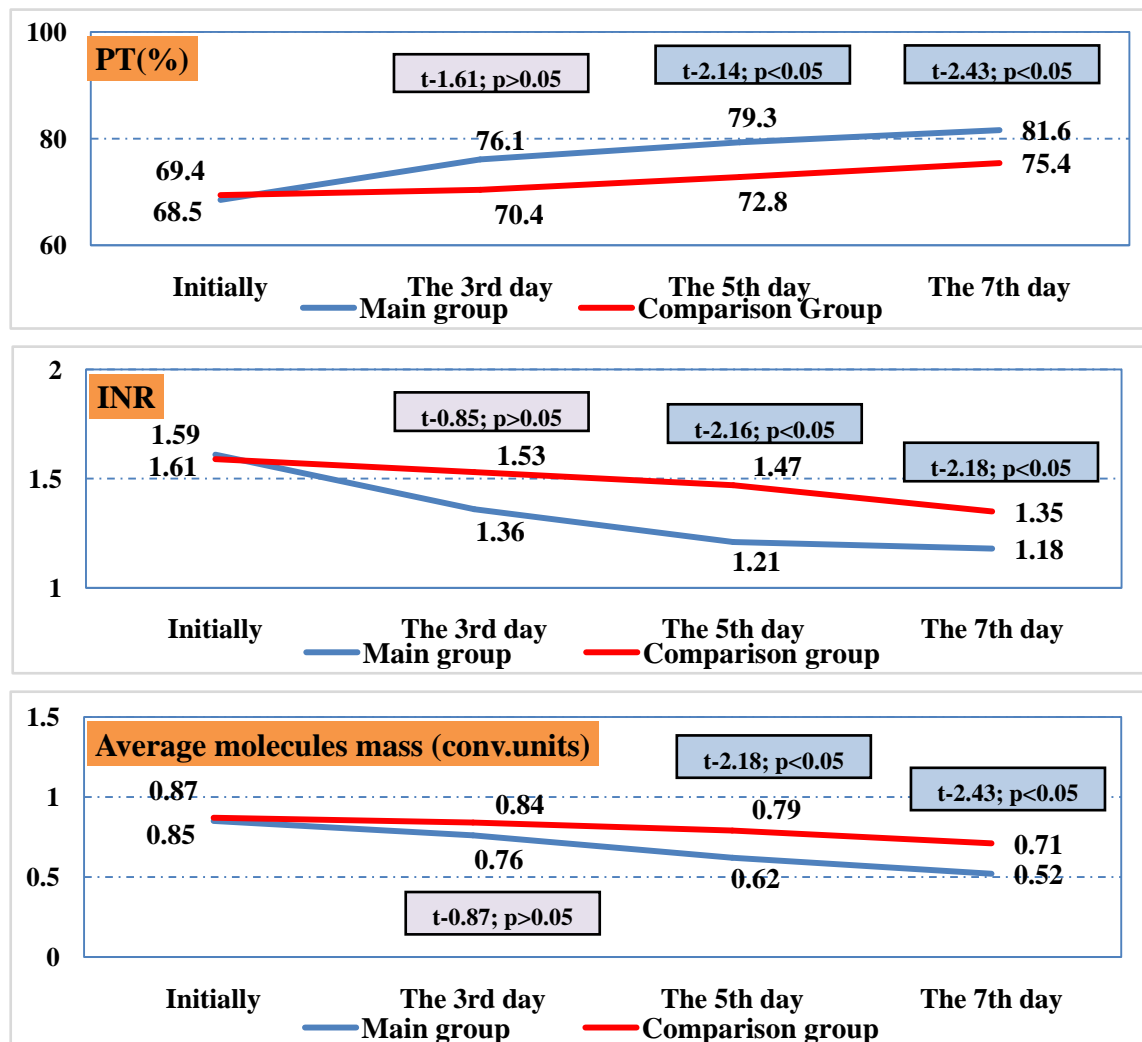
| Group            | Index                      | Total bilirubin |       |       | Points (by E.I.Galperin) |       |       |
|------------------|----------------------------|-----------------|-------|-------|--------------------------|-------|-------|
|                  |                            | Days            |       |       | Days                     |       |       |
|                  |                            | Initially       | 3     | 7     | Initially                | 3     | 7     |
| Main group       | <b>n</b>                   | 11              | 9     | 9     | 11                       | 9     | 9     |
|                  | <b>Median</b>              | 173             | 65.0  | 32.0  | 6.0                      | 2.0   | 1.0   |
|                  | <b>M</b>                   | 181.7           | 73.2  | 42.3  | 9.2                      | 3.4   | 1.2   |
|                  | <b><math>\delta</math></b> | 63.9            | 45.0  | 27.1  | 4.7                      | 4.2   | 0.4   |
|                  | <b>m</b>                   | 19.3            | 15.0  | 9.0   | 1.4                      | 1.4   | 0.1   |
|                  | <b>Maximum</b>             | 303             | 175   | 102   | 19.0                     | 14.0  | 2.0   |
|                  | <b>Minimum</b>             | 99              | 29    | 22    | 6.0                      | 1.0   | 1.0   |
| Comparison group | <b>n</b>                   | 18              | 15    | 12    | 18                       | 15    | 12    |
|                  | <b>Median</b>              | 158             | 102   | 60    | 10.0                     | 8.0   | 1.5   |
|                  | <b>M</b>                   | 180.9           | 118.3 | 78.7  | 10.9                     | 7.8   | 3.5   |
|                  | <b><math>\delta</math></b> | 80.3            | 57.7  | 47.9  | 4.7                      | 4.7   | 3.6   |
|                  | <b>m</b>                   | 18.9            | 14.9  | 13.8  | 1.1                      | 1.2   | 1.0   |
|                  | <b>Maximum</b>             | 355             | 214   | 161   | 21.0                     | 14.0  | 10.0  |
|                  | <b>Minimum</b>             | 85              | 52    | 29    | 6.0                      | 1.0   | 1.0   |
|                  | <b>t-test</b>              | -0.03           | 2.13  | 2.20  | 0.95                     | 2.33  | 2.20  |
|                  | <b>P</b>                   | >0.05           | <0.05 | <0.05 | >0.05                    | <0.05 | <0.05 |

In the main group the initial indicator of the severity of the obstructive jaundice, estimated within  $11.1 \pm 1.3$  points, decreased to  $3.5 \pm 1.0$  points on the 3<sup>rd</sup> day after treatment ( $p < 0.05$ ). On the 7<sup>th</sup> day the initial indicator decreased to  $1.8 \pm 0.4$ , in contrast to the comparison group, where this indicator decreased from the initial  $11.1 \pm 0.9$  points to  $7.4 \pm 1.0$  points on the third day, and on the 7<sup>th</sup> day after treatment - up to 3.6

$\pm 0.7$  ( $p < 0.05$ ,  $t = 2.75$  and  $2.11$ , respectively). The dynamics of the patients' condition severity after endoscopic procedure for obstructive jaundice and after traditional surgical interventions, presented in Tables 5 and 6, also traces the significant advantages of performing these interventions in patients of the main group.

**Table 6.** Dynamics of the severity of patients with obstructive jaundice after traditional surgeries

| Group            | Index          | Total bilirubin |              |             | Points (by E.I.Galperin) |             |             |
|------------------|----------------|-----------------|--------------|-------------|--------------------------|-------------|-------------|
|                  |                | Days            |              |             | Days                     |             |             |
|                  |                | Initially       | 3            | 7           | Initially                | 3           | 7           |
| Main group       | <b>n</b>       | 8               | 6            | 6           | 8                        | 6           | 6           |
|                  | <b>Median</b>  | 224.5           | 63.5         | 42.0        | 14.5                     | 1.5         | 1.0         |
|                  | <b>M</b>       | <b>228.6</b>    | <b>78.7</b>  | <b>51.5</b> | <b>13.6</b>              | <b>3.5</b>  | <b>2.7</b>  |
|                  | <b>δ</b>       | 109.6           | 45.8         | 30.1        | 5.7                      | 3.7         | 2.6         |
|                  | <b>m</b>       | 38.8            | 18.7         | 12.3        | 2.0                      | 1.5         | 1.1         |
|                  | <b>Maximum</b> | 384             | 159          | 92          | 21                       | 10          | 6           |
|                  | <b>Minimum</b> | 97              | 37           | 24          | 6                        | 1           | 1           |
| Comparison group | <b>n</b>       | 13              | 10           | 9           | 13                       | 10          | 9           |
|                  | <b>Median</b>  | 222.0           | 128.0        | 82.0        | 9.0                      | 5.5         | 2.0         |
|                  | <b>M</b>       | <b>212.7</b>    | <b>151.3</b> | <b>96.1</b> | <b>11.3</b>              | <b>6.9</b>  | <b>3.7</b>  |
|                  | <b>δ</b>       | 60.4            | 74.2         | 44.4        | 5.4                      | 6.0         | 3.0         |
|                  | <b>m</b>       | 16.8            | 23.5         | 14.8        | 1.5                      | 1.9         | 1.0         |
|                  | <b>Maximum</b> | 315             | 290          | 195         | 21                       | 21          | 10          |
|                  | <b>Minimum</b> | 133             | 58           | 42          | 6                        | 2           | 1           |
|                  | <b>t-test</b>  | <b>-0.38</b>    | <b>2.42</b>  | <b>2.32</b> | <b>-0.92</b>             | <b>1.40</b> | <b>0.69</b> |
|                  | <b>P</b>       | >0.05           | <0.05        | <0.05       | >0.05                    | >0.05       | >0.05       |



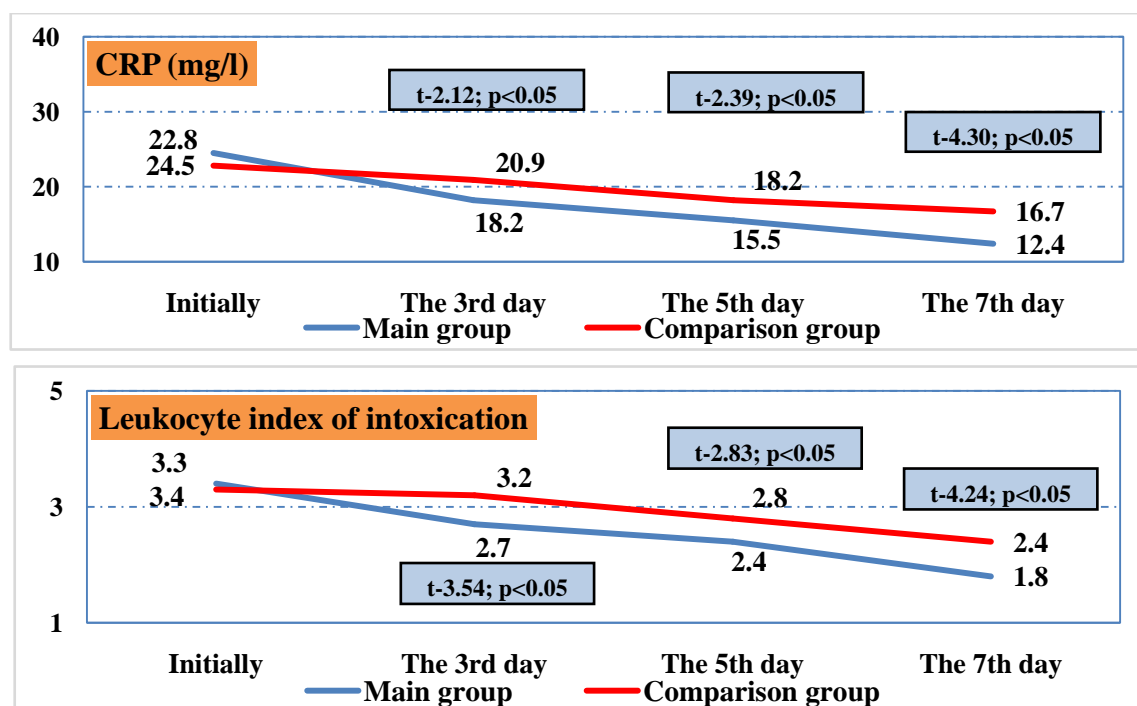


Figure 2. Dynamics of indicators of hemostasis and inflammation markers

When comparing the treatment effectiveness in both groups in terms of changes in indicators of the hemostasis and inflammation system (Fig. 2), it was noted that there was a significant positive dynamics of the coagulation system in the main group on the 5<sup>th</sup> day, in contrast to the comparison group, where these indicators slightly improved on the 7<sup>th</sup> day after treatment.

## 4. Discussions

The phenomena of endotoxemia were eliminated immediately after sessions of modified plasma adsorption in patients of the main group. It was manifested by an improvement of the clinical condition of patients and a decrease in specific indicators of intoxication and inflammation: Average molecules mass (conventional units) - from  $0.87 \pm 0.11$  to  $0.52 \pm 0.05$  on the 7<sup>th</sup> day, in contrast to the comparison group, where this indicator decreased from  $0.87 \pm 0.11$  to  $0.74 \pm 0.06$  (with a significant intergroup difference within  $t=2.43$  and  $p < 0.05$ ); C-reactive protein (CRP) (mg / l) decreased from  $24.3 \pm 1.2$  to  $12.4 \pm 0.6$  on the 7<sup>th</sup> day, in contrast to the comparison group, where this indicator decreased from  $22.8 \pm 1.4$  to  $16.7 \pm 0.8$  (with a significant intergroup difference within  $t=4.40$  and  $p < 0.05$ ); Leukocyte index of intoxication - from  $3.4 \pm 0.2$  to  $1.8 \pm 0.1$  on the 7<sup>th</sup> day, in contrast to the comparison group, where this indicator decreased from  $3.4 \pm 0.2$  to  $2.4 \pm 0.1$  ( with a significant intergroup difference within  $t=2.18$  and  $p < 0.05$ ) (Fig. 2).

## 5. Conclusions

The use of the improved technique of hyperbaric plasma adsorption in the complex treatment of the complicated course of obstructive jaundice had allowed to accelerate the regression of hyperbilirubinemia from  $201.5 \pm 19.0$  to  $75.4 \pm 11.3$   $\mu\text{mol} / \text{L}$  by the 3<sup>rd</sup> day after choledocholithiasis. At a standard conservative therapy the decrease in these indicators was from  $194.3 \pm 13.2$  to  $131.5 \pm 13.1$   $\mu\text{mol} / \text{L}$  ( $t = 3.24$ ;  $p < 0.05$ ). Accordingly, a more intense decrease in the severity of the patient's condition was noted (from  $11.1 \pm 1.3$  to  $3.5 \pm 1.0$  points versus - from  $11.1 \pm 0.9$  to  $7.4 \pm 1.0$  points;  $t = 2, 75$ ;  $p < 0.05$ ). The use of the improved technique of hyperbaric plasma adsorption also improved hemostasis indices (INR and PT with a significant improvement on the 5<sup>th</sup> day and inflammation markers (average molecules mass, C-reactive protein and leukocyte index of intoxication with a significant improvement on the 3<sup>rd</sup> -5<sup>th</sup> days).

## REFERENCES

- [1] Fargo MV, Grogan SP, Sagui A. Evaluation of Jaundice in Adults. Am Fam Physician. 2017 Feb 01; 95(3): 164-168.
- [2] Coucke EM, Akbar H, Kahloon A, Lopez PP. Biliary Obstruction. In: StatPearls. Treasure Island (FL): StatPearls Publishing; June 22, 2020.
- [3] Chen HL, Wu SH, Hsu SH, Liou BY, Chen HL, Chang MH.

- Jaundice revisited: recent advances in the diagnosis and treatment of inherited cholestatic liver diseases. *J. Biomed. Sci.* 2018 Oct 26; 25(1): 75.
- [4] Hirano R, Namazuda K, Suemitsu J, Harashima T, Hirata N. Plasma separation using a membrane. *Transfus Apher Sci.* 2017; 56(5): 649-653. doi:10.1016/j.transci.2017.08.008.
- [5] Daga Ruiz D, Fonseca San Miguel F, González de Molina FJ, et al. Plasmapheresis and other extracorporeal filtration techniques in critical patients. *Med Intensiva.* 2017; 41(3): 174-187.
- [6] Kutepov D.E. Use of extracorporeal methods of treatment of liver failure // *Kazan Medical Journal.* 2014; 95 (1). P. 75-79.
- [7] Morozov A.S. Sorbents for extracorporeal removal of toxic substances and molecules with undesirable biological activity (review) // *General Reanimatology.* 2016; 12 (6). P. 82-107.
- [8] Galperin E.I., Momunova O.N. Classification of the severity of obstructive jaundice // *Surgery*, No. 1, 2014; p. 5-9.