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THE PROGNOSTIC VALUE OF HEMODYNAMICS INDICES AND BIOMARKERS I-FABP AND L-FABP IN ABDOMINAL COMPARTMENT SYNDROME IN CHILDREN WITH ACUTE NEUROINFECTIONS

Abstract. *Introduction. Infectious diseases in children may be associated with risk factors of developing of intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS). Material and methods. We conducted a retrospective study of cases of ACS in children with infection diseases. Parameters of central and peripheral hemodynamic assessed by echocardiography and doppler ultrasound, and biochemical markers (I-FABP, L-FABP, ALT, bilirubin, creatinine, BUN) were evaluated. Results. Seven cases of ACS and IAH were investigated. Increased abdominal pressure and ACS were associated with significant elevation of serum creatinine (81,37±35,92 mcmol/l amid elevated IAP and 57,14±19,63 in normal IAP, p<0,05), intestinal serum biomarker I-FABP (13,44±4,58 ng/ml amid elevated IAP and 2,65±1,25 amid normal IAP), higher cardiac output (6,0±0,57 l/min/m2 vs 4,3±0,34 l/min/m2 in normal IAP, p<0,05), decreased diastolic blood flow velocity in renal and superior mesenteric arteries (3,4±1,08 cm/s vs 18,7±1,58 cm/s in renal arteries, 5,1±0,87 cm/s vs 17,5±3,90 cm/s in superior mesenteric artery, p<0,05), and elevated peripheral resistance index (RI) in the renal artery (0,92±0,02 vs 0,70±0,02, p<0,05). Conclusion. Assessment of biochemical tests and hemodynamic parameters may be used as additional diagnostic tool for children with ACS.*
Keywords: *abdominal compartment syndrome, FABP, hemodynamic, children.*

Introduction. Abdominal compartment syndrome (ACS) is a rarely diagnosed serious condition that can complicate the course of different diseases. It is believed that among children who receive therapy in intensive care units, the frequency of ACS fluctuates at the level of 0.6-4.7%, while the mortality rate reaches 40-60%[1]. Currently, diseases with a high risk of intra-abdominal hypertension (IAH) and abdominal compartment include trauma, intestinal obstruction, necrotic enterocolitis, abdominal wall defects, diaphragmatic hernia and septic shock with massive intravenous infusion[2]. In cases of acute infectious of the central nervous system (CNS) in children, the frequency of IAH and ACS has not yet been studied.

Purpose of the study. Estimate prognostic value of biochemical markers and hemodynamic indices in the diagnosis of abdominal compartment syndrome in children with acute CNS infections.

Material and methods. Retrospective chart review of children with abdominal compartment syndrome who were treated in the intensive care unit of the municipal children's infectious diseases hospital in 2015-2017 due to acute neuroinfections. Cases of a documented increase in abdominal pressure and symptoms of abdominal compartment were selected for further analysis. ACS in patients was determined according to the criteria of the World Association for Abdominal Compartment Syndrome (2013). Intra-abdominal pressure (IAP) was determined in the presence of risk factors for the development of IAH and ACS. Patients' intra-abdominal pressure was measured using a standard bladder catheter. Increased pressure was considered to be more than 10 mm Hg[2]. ACS was diagnosed in cases of steady increase in abdominal pressure of more than 10 mm Hg and the appearance of organ

dysfunctions. The presence of organ dysfunction was determined according to the criteria described in the International pediatric sepsis consensus conference (2005) and the logistic scale of organ dysfunction PELOD (1999). To determine the intensity of injury of organs of the gastrointestinal tract, the level of biomarkers I-FABP and L-FABP was investigated[3]. As part of an additional examination, according to local protocols, the intensive care unit also conducted a study of central and peripheral hemodynamics using echocardiography and Doppler ultrasound (DUS). The ultrasound machine Siemens Sienna with convex sensors 5-7.5 MHz and 3.5-5 MHz and a linear sensor 7.5 MHz. An echocardiographic study was performed transthoracically with the calculation of the end-diastolic and end-systolic volumes of the left ventricle with the subsequent calculation of the stroke volume (SV) according to Teichholz (1976), the systolic index (SI) and the ejection fraction (EF). Preloading of the left ventricle was assessed by the end-diastolic diameter (EDD) of the left ventricle. DUS was carried out according to a standard method with the determination of systolic (V max) and diastolic (V min) blood flow rates, the index of peripheral resistance RI (RI = (Vmax-Vmin)/Vmax) was calculated. The characteristics of blood flow in the abdominal aorta, renal arteries, superior mesenteric artery, celiac trunk, and posterior tibial artery were studied.

Results. We analyzed 53 case histories of children in the intensive care unit with a diagnosis of acute neuroinfection. Among them, there were 42 patients with bacterial meningitis, 10 patients with encephalitis and 1 patient with viral meningitis. We selected 6 cases from this group that met the criteria of abdominal compartment syndrome in the form of a registered increase in abdominal pressure with the concomitant appearance of organ and system dysfunction. The maximum registered value of abdominal pressure is 26 mm Hg. The age of patients was from 1 month to 10 years. Boys - 4 (57.1%), girls - 3 (42.9%). 3 children were diagnosed with unspecified bacterial meningitis, 2 children were diagnosed with generalized meningococcal infection (meningitis and coccemia), 1 child was diagnosed with viral encephalitis (unspecified ethiology). In 2 children, increased intra-abdominal pressure and clinical manifestations of abdominal compartment were observed during hospitalization; these symptoms have been developed in 3 children within two to three days, in another one - after the 10th day of stay in the intensive care unit. The duration of the period of increased intra-abdominal pressure ranged from 3 to 6 days (median - 4 days). The development of ACS in all 6 patients was accompanied by the development of acute renal dysfunction, in 4 patients - with neurological disorders (depression of consciousness), in 2 patients - with associated respiratory dysfunction, in 3 patients - with coagulation hemostasis, in all 6 patients - with inhibition of intestinal peristaltic activity with a significant amount of gastric stasis. An ultrasound examination revealed free fluid in the abdominal cavity in all 6 patients, in addition in the pleural cavity – in 3 patients and in the pericardial cavity in 3 patients. In all patients, conservative tactics (nasogastric and rectal drainage, early enteral feeding, adequate sedation, correction of infusion therapy and providing negative fluid balance) were used in the treatment of intra-abdominal hypertension. In all the studied patients, a positive trend was observed during treatment, there were no fatal cases.

Laboratory and instrumental studies were conducted in all patients over time and covered both the period of intra-abdominal hypertension and after normalization of abdominal pressure during therapy. Further, we compared the indices obtained in the days when IAP was increased, with the same indices obtained after the normalization of IAP. The results of biochemical studies in patients at different periods of the disease are shown in Table 1.

Table 1.

Biochemical markers (M ± SD) in the period of normal and increased IAP

Index	High IAP	Normal IAP
pH	7,40±0,07	7,37±0,08
BE, mmol/L	-2.31±6,06	-1,47±5,97
Creatinine, µmol/l	81,37±35,92*	57,14±19,63*
Urea, mmol/L	13,07±11,48	6,47±2,81
ALT, U/l	76,21±47,14	66,30±70,57
Bilirubin, µmol/l	14,66±4,24	16,18±0,93
I-FABP, ng/ml	13,44±9,16*	2,65±2,49*
L-FABP, ng/ml	355,03±325,86	156,16±82,11

** - significant difference between groups (p <0.05 according to the Mann-Whitney criterion)*

The average pH level in observed patients varied between 7.22–7.54. Episodes of decompensated acidosis were reported in 5 of 7 patients, and two children had an increase in pH above 7.45. There were no significant differences in pH between episodes on the background of increased and normal abdominal pressure. The deficit of bases for BE varied widely (from -14.40 to 10.10 mmol/l). The average BE indexes on the background of increased and normal IAP did not differ significantly. The creatinine index was recorded in the range of 35 - 158 µmol/l. An increase in creatinine above the age norm was observed in 6 out of 7 patients. A higher average creatinine level was recorded in children during the period of increased IAP, lower creatinine level was recorded at normal IAP level (p=0.04363, according to Mann-Whitney criterion). The average urea level was also slightly higher during the period of IAP increase, but the difference in comparison with the urea level at the normal IAP value was insignificant (p>0.05). ALT levels in patients ranged from 12.0 U/l to 280.0 U/l. A significant increase in ALT (more than 2 norms) was observed in three children, including one patient was diagnosed with bacterial meningitis and two patients - with encephalitis. There was no significant difference between ALT levels at increased and normal IAP levels (p>0.05, according to Mann-Whitney criterion). Total bilirubin in our patients ranged from 9.8 to 229.9 µmol/l. There was no significant difference between the indicators at increased and normal IAP (p>0.05). Among the study group of patients, an increase in bilirubin level above the normal level was observed only in a patient with viral encephalitis. I-FABP level, when measured during increased IAP, averaged 13.44 (from 3.91 to 25.54 ng/ml), and 2.65 against the background of normal IAP (from 0.1 to 5.8 ng/ml) (p = 0.03662, according to Mann-Whitney criterion). L-FABP was also higher in patients with increased IAP (355.03, 145.93 to 914.53 ng/ml) than in patients after IAP normalization (156.16 ng/ml, 37.16 to 251.02 ng/ml) (p>0.05).

The average values of central hemodynamics obtained against the background of normal and increased intra-abdominal pressure are presented in table 2.

The systolic blood pressure in patients against the background of increased IAP and the development of ACS did not change significantly and did not go beyond the age norm. Diastolic pressure during increased IAP tended to decrease in all patients, but these changes were statistically insignificant (p>0.05 according to Mann-Whitney criterion). The index of contractile function of the left ventricle (EF) during the development of ACS did not change significantly. In all patients with increased IAP and development of ACS, an increase in cardiac output was observed. The average systolic index was significantly higher compared with the determination during the period of normal IAP (p = 0.028 according to Mann-Whitney criterion).

Indicators of arterial blood flow in peripheral vessels, obtained in the period of increased and normal IAP, are shown in table 3.

Table 2.

Central hemodynamic indices (M±SD) in the period of normal and increased IAP levels

Index	High IAP	Normal IAP
sBP, mm Hg	96,2±13,47	105,5±23,13
dBP, mm Hg	52,6±13,70	62,2±21,76
SI, l/min/sq	6,0±2,13*	4,3±1,97*
EF, %	68,0±10,56	66,6±10,38

sBP - systolic blood pressure, dBP - diastolic blood pressure, SI - systolic index, EF - ejection fraction.

Table 3.

Peripheral hemodynamic indices (M±SD) at normal and increased IAP levels

Vessel/index	High IAP	Normal IAP
Abdominal aorta		
V max, m/s	145,6±68,1	142,9±52,6
V min, m/s	6,3±6,5	11,7±7,5
Renal artery		
V max, m/s	54,1±33,9	66,5±28,8
V min, m/s	3,4±4,0*	18,7±7,9*
Celiac trunk		
V max, m/s	115,7±40,2	124,3±58,2
V min, m/s	22,1±16,2	33,7±14,9
Superior mesenteric artery		
V max, m/s	148,8±112,2	162,7±74,8
V min, m/s	5,1±2,5*	17,5±16,1*
Posterior tibial artery		
V max, m/s	34,6±18,7	30,9±14,5
V min, m/s	2,4±5,2	2,4±3,1

** - significant difference between groups (p <0.05 according to the Mann-Whitney criterion).*

The mean systolic velocity (V max) in the abdominal aorta did not differ significantly during increased and normal abdominal pressure. The diastolic velocity (V min) with an increased IAP tended to decrease, however, the difference in the average indices was unreliable (p> 0.05). In the renal and superior mesenteric arteries, systolic and diastolic blood flow velocity decreased against the background of abdominal hypertension. Most of the changes were related to diastolic velocity, and the difference between the mean values of V min was significant (p<0.001, according to Mann-Whitney criterion). In addition, the peripheral resistance index (RI) in the renal artery on the background of IAH significantly increased to 0.92±0.086, compared with the level at normal IAP - 0.70±0.112 (p<0.00001 according to Mann-Whitney criterion). In the celiac trunk, there was a tendency to a decrease in both systolic and diastolic velocities, but there was no significant difference between the averages. The average values of V max and V min in the posterior tibial artery practically did not differ from the results obtained at normal abdominal pressure (p> 0.05).

Discussion. The frequency of abdominal compartment syndrome in the intensive care unit among children with acute infectious lesions of the central nervous system was 13.2%, which is comparable to the frequency of this syndrome in non-infectious patients[1]. In this paper, we investigated which laboratory and instrumental studies indicators are more closely related to abdominal hypertension and abdominal compartment syndrome. Among the biochemical markers, we identified a correlation between the increase in IAP with an increase in the level of biomarkers I-FABP and L-FABP[4]. At the same time, we observed high levels of these indices in three patients even before the onset of symptoms of increased abdominal pressure. This confirms the view that the starting factor of abdominal hypertension, as a rule, are disorders of the gastrointestinal organs[2].

In the pathogenesis of abdominal compartment, an increase in the peripheral resistance of the abdominal vessels with a subsequent drop in cardiac output and a decrease in blood pressure also plays an important role[5]. However, against the background of abdominal hypertension, we noted in our patients only statistically insignificant multidirectional changes in blood pressure. The absence of correlation of blood pressure with IAH is noted by the authors of other studies[6]. High abdominal pressure and a decrease in venous return theoretically should lead to a drop in cardiac output. However, an increase in abdominal pressure in our patients was associated with a significant increase in cardiac output. In our opinion, this may be due to the fact that septic diseases are more often associated with normal or increased cardiac output due to tachycardia, reduced afterload and the use of intensive infusion therapy[7]. It is also possible that an increase in IAP among our patients did not reach a certain “critical” level, after which cardiac output should decrease.

Changes in the regional blood flow, in particular in the renal and superior mesenteric arteries, with an increase in abdominal pressure were unidirectional. According to the literature, the blood flow in the renal arteries responds rather early to an increase in IAP. Among the indicators of blood flow, the resistance index (RI) in the renal arteries demonstrates a large correlation. According to the results of its observations, Umgelter A et al reports a significant increase in RI in the renal arteries with an increase in abdominal pressure up to 20 mm Hg[8]. Experimental data published in the literature also indicate that an increase in intra-abdominal pressure leads to a decrease in diastolic velocity in the mesenteric artery, which coincides with our results[9].

Conclusions. The development of acute renal failure and accumulation of free fluid in the abdominal cavity are characteristic of the abdominal compartment syndrome in children with acute neuroinfections. ACS is characterized by an increase in the level of creatinine from biochemical blood markers, as well as biomarkers I-FABP and L-FABP. Among the hemodynamic indices, a decrease in diastolic linear velocity and an increase in peripheral resistance index (RI) in the renal and superior mesenteric arteries has a higher prognostic value for the diagnosis of intra-abdominal hypertension and abdominal compartment syndrome, as well as an increase in cardiac output.

Prospects for further research. The main limitations of our study are small sample cohort and single-centre design. Future multicenter trials

with large number of patients can determine precision values of hemodynamic and biomarkers parameters that may be used for early diagnosis of abdominal compartment syndrome in children with acute CNS infection.

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