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INTESTINAL ALKALINE PHOSPHATASE — A BIOMARKER OF THE DEGREE OF ACUTE ENTERAL INSUFFICIENCY IN URGENT SURGERY

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ABSTRACT — The diagnostic significance for levels of alkaline phosphatase (ALP) and intestinal alkaline phosphatase (IAP) and their ratio in blood serum and intestinal contents were compared to assess the degree of acute enteral insufficiency in urgent surgical pathology complicated by peritonitis. The results of examination of 112 patients with acute surgical pathology complicated by peritonitis were retrospectively analyzed. Biochemical data were compared with clinical and instrumental data obtained by ultrasonography and Doppler flowmetry. The main statistical indicator was Spearman's rank correlation coefficient, which showed a moderate direct correlation in patients with stage I and II enteral insufficiency ($r=0.63$ at $p\leq0.05$), and in the group with st. III it showed a direct correlation with a high closeness of association ($r=0.71$ at $p\leq0.05$). The IAP/ALP ratio makes it possible to objectively assess the severity of acute intestinal failure in urgent surgery.

KEYWORDS — peritonitis, acute intestinal failure, biomarkers, intestinal alkaline phosphatase, intestinal homeostasis.

RELEVANCE

Acute enteral insufficiency (AEI) is the most common clinical syndrome in acute surgical pathology and peritonitis. The frequency of AEI according to different authors ranges from 30 to 94%. The severity of AEI is diagnosed intraoperatively, as well as using rather expensive devices that assess the degree of morpho-functional dysfunction of the small intestine [1, 2]. Currently, there are no rapid biochemical tests to assess the degree of AEI in the preoperative and postoperative periods.

Alkaline phosphatases (ALPs) are a group of isoenzymes located on the outer layer of the cell membrane; they catalyze the hydrolysis of organic phosphate esters present in the extracellular space. Intestinal alkaline phosphatase (IAP) is a multifunctional protein that has been shown to primarily protect the intestinal mucosa [3, 4, 5, 6]. The role of IAP in maintaining intestinal homeostasis is highlighted by the observation that IAP expression is impaired in many gastrointestinal disorders such as inflammatory bowel disease, necrotizing enterocolitis, and metabolic syndrome. Besides, exogenous IAP supplementation improves outcomes associated with these disorders [7, 8, 9, 10]. A recently identified new function of IAP is the induction of autophagy [11, 12]. Due to its critical role in gastrointestinal physiology and excellent safety profile, IAP has been used in clinical trials to treat many critical conditions, including those associated with sepsis [13, 14, 15].

The aim of the work was to compare the diagnostic significance of the levels of alkaline ALP and IAP and their ratio in blood serum and intestinal contents for estimation of the degree of AEI in urgent surgical pathology complicated by peritonitis.

MATERIAL AND METHODS

A retrospective analysis of the results of examination of 112 patients with acute surgical pathology of the abdominal organs complicated by peritonitis and varying degrees of AEI was carried out. 26 patients were diagnosed with stage I AEI, 38 had stage II, and 48 — stage III decompensated AEI. The total ALP (U/l), its isoform IAP (U/l), as well as their IAP/ALP ratio (%) in blood serum and intestinal contents were determined using the enzyme immunoassay method and the Cobas e411 apparatus (Switzerland). Studies were carried out before surgery, on days 1–3 and 5–7. In order to summarize and compare the data we collected, the stage of AEI was subsequently assessed visually and intraoperatively, by calculating the enteral morpho-functional coefficient (EMFC), as well as data obtained using enteral laser Doppler flowmetry (ELDF).

EMFC was assessed after ultrasonography by the formula: $EMFC = Tst(k) \times D(k)/FPD$ in 1 minute,

where: Tst(k) — thickness of the intestinal wall (mm); D(k) - intestine diameter (mm); FPV — the frequency of peristaltic movement of the intestine in 1 minute. With a value of up to 5 points, it was defined as the stage I of compensation. From 5 to 25 points, stage II of subcompensation was detected, and with an EMFC value above 25 points, stage III of decompensation was diagnosed.

ELDF was performed with the analyzer of microcirculation and microlymph flow "Lasma MTs-1" (Russia). Investigated: percentage of microcirculation (PM; p.u.); standard deviation (SD; σ, p.u.), as well as the coefficient of variation (CV; %).The obtained results were compared with the reference values of abdominal microcirculation obtained in patients during elective operations for non-inflammatory diseases of the abdominal organs.

In order to identify and evaluate the tightness of the relationship between quantitative indicators, the Spearman rank correlation coefficient was calculated, which allowed to check the heteroscedasticity of random errors in the regression model. To determine the significance of p differences between groups, Student's t test and one-way analysis of variance with Fisher's F test were used. Differences were considered statistically significant at $p \leq 0.05$.

RESULTS AND DISCUSSION

At stage I AEI, the level of ALP in the blood serum was 213±29.2 U/l, in the intestinal chyme - 38±9.2 U/l; IAP was 1.18±0.74 U/l and 1.24±0.19 U/l, IAP/ALP ratio was 0.55±0.27% and 3.26±0.27%, respectively. At stage II, ALP in serum was 295±28.4 U/l, in chyme — 95±13.4 U/l, IAP values were 1.87±0.46 U/l and 3.86±0.93 U/l, and the IAP/ALP ratio was 0.63±0.29% and 4.06±0.29%, respectively. At stage I III, the total serum ALP was 341±33.3 U/l, in the intestinal contents — 141±17.3 U/l, the IAP values were 2.29±0.53 U/l and 4.31±1.49 U/l, IAP/ALP were 0.67±0.15% and 6.05±0.15%, respectively.

Thus, as AEI progressed, there was an increase in the levels of ALP and IAP in the blood serum and intestinal chyme. These data correlated with those obtained with EMFC and ELDF. With stage I AEI, the average score for EMFC calculation was 4.7±0.3, with stage II — 16.6±1.2, and with stage III — 27.4±2.2 points. ELDF indices indicated a progressive increase in pre- and post-capillary resistance, arteriolo-venular shunting, which ultimately led to severe perfusion disorders of the intestinal wall (Table 1).

With the ratio of the obtained clinical-instrumental and biochemical data, it turned out that the most informative biochemical indicator was the IAP/ALP ratio. Spearman's rank correlation coefficient for this indicator showed a moderate direct correlation in patients with stage I and II. AEI ($r=0.63$ at $p \leq 0.05$). In the group with stage III AEI score IAP/ALP showed a direct correlation with a high closeness of association ($r=0.71$ at $p \leq 0.05$).

CONCLUSIONS

The biochemical indicator IAP/ALP allows an objective assessment of the stage of AEI in patients with acute diseases of the abdominal organs complicated by peritonitis. This hypothesis was confirmed by clinical and instrumental data obtained with EMFC and ELDF. Biochemical monitoring of the IAP/ALP ratio allows diagnosing the stage of AEI both in the preoperative and postoperative periods, assessing the effectiveness of therapy and making timely corrections to the treatment.

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Table 1. *Biochemical and clinical-instrumental parameters in patients with peritonitis depending on the degree of acute intestinal failure (M±m; abs)*

AEI stage (n=112)	Object of study	ALP (ЕД/л)	IAP (ЕД/л)	IAP/ALP (%)	EMFC (points)	ELDF: (PM (p.u.) ; SD(p.u.); CV (%)
I (n=26)	serum	213±29,2	1,18±0,74	0,55±0,27*	4,7±0,3	32,21±1,18
						5,42±0,33
	intestinal chyme	38±9,2	1,24±0,19	3,26±0,27*		12,64±1,50
II (n=38)	serum	295±28,4	1,86±0,46	0,63±0,29*	16,6±1,2	23,3±1,83
	intestinal chyme	95±13,4	3,86±0,90	4,06±0,29*		3,69±0,15
						11,34±4,04
III (n=48)	serum	341±33,3	2,29±0,53	0,67±0,15*	27,4±2,2	17,6±1,55
	intestinal chyme	141±17,3	4,31±1,49	6,05*±0,15*		2,03±0,19
						6,03±3,79

Note: ** — indicators at p≤0.05*

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