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INTERRELATION OF INTRAABDOMINAL HYPERTENSION AND MARKERS OF GASTROINTESTINAL TRACT INJURY IN PATIENTS WITH MULTIORGAN DYSFUNCTION

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Abstract

Relevance. Intraabdominal hypertension syndrome is one of the main causes in the etiology of multiorgan dysfunction and high mortality of patients. It is relevant today to determine the level of the interrelation of various markers of bacterial translocation (presepsin and I-FABP) and IAH for the purpose of early diagnosis of complications since there are not enough studies.

Aim: Analysis of available data on the correlation between IAH and bacterial translocation in various-genesis critically ill patients.

Question: Is there a correlation between IAH and bacterial translocation markers in critically ill patients?

Search strategy: Sources of information: Pubmed, Scopus, Google Scholar, Web of Science for the last 10 years (from 2013 to 2023). *Inclusion criteria:* all research papers that included patients with multiple organ dysfunction, abdominal hypertension, and surgical diseases of the gastrointestinal tract. Patients in intensive care units who underwent detection of bacterial translocation proteins, particularly, I-FABP, presepsin, and zonulin. In addition, experimental papers with animals using the same criteria over the past 10 years. *Exclusion criteria:* studies that were published before 2013, as well as studies that did not have the main search criteria (abdominal hypertension, multiple organ dysfunction, markers of bacterial translocation were not detected). Patients under 18 years of age, patients with bladder injury or cancer. *Key requests:* multiple organ dysfunction, abdominal hypertension, intra-abdominal hypertension syndrome, I-FABP, presepsin, zonulin, gastrointestinal diseases, sepsis, multiple organ failure. Considering the uniqueness of the study, 88 papers were identified and selected according to the search strategy.

Results: Presepsin levels vary in healthy patients, SIRS patients, and patients with diagnosed sepsis within the range of 258.7±92.53ng/L, 430.0±141.33ng/L, and 1,508.3±866.6ng/L, respectively. In patients with acute surgical diseases, the level of I-FABP protein is much higher than in patients of the control group.

The relevance of determining the level of zonullin protein in the blood in patients with multiorgan dysfunction is controversial and requires further in-depth research.

Conclusion: According to the study, the relationship between the level of intra-abdominal hypertension and the proteins presepsin and I-FABP was determined in patients with multi-organ dysfunction of various origins. Study levels of presepsin, zonullin and I-FABP proteins in patients with multiorgan dysfunction due to their minimally invasive nature and rapidness of execution, contribute to reducing the mortality rate from postoperative complications, as well as timely surgical treatment.

Keywords: *intraabdominal hypertension, presepsin, I-FABP, multiorgan dysfunction, abdominal surgery, abdominal compartment syndrome.*

Резюме

ВЗАИМОСВЯЗЬ ВНУТРИБРЮШНОЙ ГИПЕРТЕНЗИИ И МАРКЕРОВ ПОРАЖЕНИЯ ЖЕЛУДОЧНО-КИШЕЧНОГО ТРАКТА У БОЛЬНЫХ С ПОЛИОРГАННОЙ ДИСФУНКЦИЕЙ

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Актуальность. Синдром интраабдоминальной гипертензии является одной из главных причин в этиологии полиорганной недостаточности и высокой смертности пациентов. Актуальным на сегодняшний день является определение уровня взаимосвязи различных маркеров бактериальной транслокации (пресепсин и I-FABP) и ИАГ с целью ранней диагностики осложнений, так как исследований мало.

Цель: Проведение анализа имеющихся данных литературы о корреляции ИАГ и бактериальной транслокации у пациентов в критическом состоянии различного генеза.

Вопрос: имеется ли корреляция между ИАГ и маркерами бактериальной транслокации у пациентов в критическом состоянии?

Стратегия поиска: Источники информации: Pubmed, Scopus, Google Scholar, Web of Science за последние 10 лет (с 2013 по 2023 г). *Критерии включения:* все исследовательские работы, в которых фигурировали пациенты с мультиорагнной дисфункцией, абдоминальной гипертензией, хирургическими заболеваниями желудочно-кишечного тракта. Пациентов, находящихся в палатах интенсивной терапии, которым проводилось определение белков бактериальной транслокации, в частности I-FABP, пресепсина, зонулина. А так же экспериментальные работы с животными по тем же критериям за последние 10 лет. *Критерии исключения:* исследования, которые публиковались до 2013 года, а так же работы в которых не было основных критериев поиска (абдоминальная гипертензия, мультиорганная дисфункция, не определялись маркеры бактериальной транслокации). Пациенты до 18 лет, пациенты с травмой мочевого пузыря или онкологическими заболеваниями. Ключевые запросы: мультиорганная дисфункция, абдоминальная гипертензия, синдром интраабдоминальной гипертензии, I-FABP, пресепсин, зонулин, заболевания желудочно-кишечного тракта, сепсис, полиорганная недостаточность. Учитывая уникальность исследования были выявлены и отобраны 154 статей согласно стратегии поиска. Из 154 работ были рассмотрены 88 статьи относящихся к теме данной работы.

Результаты: Уровень пресепсина варьирует у здоровых, SIRS, и у пациентов с диагностированным сепсисом в пределах 258,7±92,53 нг/л, 430,0±141,33 нг/л, 1508,3±866,6 нг/л соответственно. У пациентов с острыми хирургическими заболеваниями уровень белка I-FABP намного выше, чем у пациентов в контрольной группе.

Актуальность определения уровня белка зонуллина в крови у пациентов с мультиорганной дисфункцией спорное и требует дальнейших углубленных исследований.

Заключение: Согласно проведенному исследованию, определена взаимосвязь между уровнем интраабдоминальной гипертензии и белками пресепсин и I-FABP у пациентов с мультиорагнной дисфункцией различного генеза. Исследуемый уровень белков пресепсин, зонуллин и I-FABP у пациентов с мультиорганной дисфункцией ввиду малоинвазивности и быстроты выполнения способствуют снижению уровню смертности от послеоперационных осложнений, а так же своевременному хирургическому лечению.

Ключевые слова: *интраабдоминальная гипертнзия, пресепсин, I-FABP, мультиорганная дисфункция, абдоминальная хирургия, абдоминальный компартмент синдром.*

Түйіндеме

КӨП АҒЗАЛЫ ДИСФУНКЦИЯСЫ БАР НАУҚАСТАРДАҒЫ ИНТРААБДОМИНАЛЬДЫ ГИПЕРТЕНЗИЯ МЕН АСҚАЗАН-ІШЕК ЖОЛДАРЫНЫҢ ЗАҚЫМДАНУ МАРКЕРЛЕРІНІҢ ӨЗАРА БАЙЛАНЫСЫ

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Өзектілігі: Интраабдоминальды гипертензия синдромы көп мүшелі жеткіліксіздік этиологиясының және пациенттердің жоғары өлімінің негізгі себептерінің бірі болып табылады. Бүгінгі таңда асқынуларды ерте диагностикалау мақсатында бактериялық транслокацияның әртүрлі маркерлерінің (пресепсин және i-FABP) және ИАГ арасындағы байланыс деңгейін анықтау өзекті болып табылады, өйткені зерттеулер аз.

Мақсат: Әртүрлі генездің ауыр жағдайындағы пациенттерде ИАГ корреляциясы және бактериялық транслокация туралы қолда бар деректерге талдау жүргізу.

Сұрақ: ауыр науқастарда ИАГ және бактериялық транслокация маркерлері арасында корреляция бар ма?

Іздеу стратегиясы: Ақпарат көздері: соңғы 10 жылдағы Pubmed, Scopus, Google Scholar, Web of Science (2013 жылдан 2023 жылға дейін). *Қосылу критерийлері:* көп ағзалы дисфункциясы, абдоминальды гипертензия және асқазан-ішек жолдарының хирургиялық аурулары бар пациенттерді қамтитын барлық зерттеу жұмыстары. Бактериялық транслокациялық ақуыздарды, атап айтқанда I-FABP, пресепсин, зонулинді анықтаудан өткен реанимация бөлімшелеріндегі науқастар. Сондай-ақ соңғы 10 жыл ішінде бірдей критерийлерді қолданатын жануарлармен эксперименталды жұмыс. *Алып тастау критерийлері:* 2013 жылға дейін жарияланған зерттеулер, сондай-ақ негізгі іздеу критерийлері жоқ зерттеулер (абдоминальды гипертензия, көп ағзалардың дисфункциясы, бактериялық транслокация маркерлері анықталмаған). 18 жасқа толмаған науқастар, қуық жарақаты немесе қатерлі ісігі бар науқастар. *Негізгі сұрақтар:* көп ағзалы дисфункция, абдоминальды гипертензия, интраабдоминальды гипертензия синдромы, I-FABP, пресепсин, зонулин, асқазан-ішек аурулары, сепсис, көп мүше жеткіліксіздігі. Зерттеудің бірегейлігін ескере отырып, іздеу стратегиясы бойынша 88 мақала анықталып, іріктелді.

Нәтижелер: Пресепсин деңгейі сау, SIRS және сепсис диагнозы қойылған науқастарда сәйкесінше 258,7±92,53 нг/л, 430,0±141,33 нг/л, 1508,3±866,6 нг/л аралығында өзгереді. Жедел хирургиялық аурулары бар науқастарда i-FABP ақуызының деңгейі бақылау тобындағы науқастарға қарағанда әлдеқайда жоғары.

Көп органикалық дисфункциясы бар науқастарда қандағы зонуллин ақуызының деңгейін анықтаудың өзектілігі даулы болып табылады және одан әрі терең зерттеулерді қажет етеді.

Қорытынды: Зерттеуге сәйкес интраабдоминальды гипертензия деңгейі мен пресепсин мен I-FABP белоктары арасындағы байланыс әр түрлі шығу тегі көп ағзалардың дисфункциясы бар науқастарда анықталды.Зерттеуге сәйкес, интраабдоминальды гипертензия деңгейі арасындағы байланыс анықталды. - абдоминальды гипертензия және әр түрлі шығу тегі көп ағзалы дисфункциясы бар емделушілерде пресепсин және I-ФАБП белоктары.

Көп органикалық дисфункциясы бар емделушілерде пресепсин, зонуллин және I-FABP ақуыздарының деңгейін зерттеу аз инвазивтілік пен орындалу жылдамдығына байланысты операциядан кейінгі асқынулардан болатын өлім-жітім деңгейін төмендетуге, сондай-ақ уақтылы хирургиялық емдеуге ықпал етеді.

Түйін сөздер: *абдоминальды гипертензия, пресепсин, i-FABP, көп мүшелі дисфункция, абдоминальды хирургия, абдоминальды компартмент синдромы.*

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Introduction

According to the definition approved in the international protocol of the World Society of the Abdominal Compartment Syndrome (WSACS) (The Abdominal Compartment Society, 2013), intra-abdominal hypertension (IAH) is defined as an established or recurrent pathological increase in intraabdominal pressure (over 12 mmHg) [1,3]. Based on the WSACS (The Abdominal Compartment Society, 2013) protocol, intra-abdominal hypertension syndrome is one of the main causes in the etiology of multiple organ dysfunction and high mortality of patients [2,3,46]. Intra-abdominal pressure (IAP) is normally a reflection of intrapleural pressure and is zero or moderately negative (below atmospheric). Intra-abdominal hypertension (IAH) is common for critically ill patients in the ICU and is also an independent predictor of mortality. The main cause of mortality in the case of IAH is the translocation of intestinal bacteria and the development of abdominal sepsis. Many studies conducted under the control of Intensive Care Units (ICU) have shown that patients in the ICU, regardless of the underlying disease, suffer from IAH in 50% of cases [4,5, 50].

An increase in abdominal pressure to the lower normal limit (i.e. up to 10-12 mmHg) can be observed with an increase in waist size (one of the indicators of obesity, since the diaphragm and portal vein are compressed), as well after laparoscopic manipulations [5,6,48]. The persistence of high level of abdominal pressure leads to compartment syndrome. Therefore, in closed abdominal cavity it interrupts the normal blood supply to the abdominal organs, after which appears necrosis of the internal organs. [1,7].

In the case of peritonitis, pancreatic necrosis, and severe combined trauma, a significant increase in pressure was noted in 30% of patients, and the development of IAHS in 6% of such patients [7,8,51].

The main purpose of this paper is to analyze the available data on the correlation between IAH and markers of gastrointestinal injury in patients with multiple organ dysfunction.

Multiple organ dysfunction syndrome (MODS) or multiple organ failure is characterized by the dysfunction of two or more organs due to infection, shock, or injury [9]. There are several scoring systems developed to assess the severity of a patient's condition, one of the first is the MOF (Multiple Organ Failure) scoring system, which uses points to determine the state of the systems, i.e. respiratory, cardiovascular, urinary, hepatobiliary, hematological, gastrointestinal, or nervous. In addition, no less relevant is the SOFA (Sepsis-Related Organ Failure) scoring system, which was created to quickly calculate and describe complications in critically ill patients caused by multiple organ failure with septic syndrome [3,26].

Sepsis induces MODS, damaging organs at the cellular level, disrupting the regulation of the immune response, and forming organic damage [10,11]. Using the example of the gastrointestinal tract, it is worth noting that there are very few papers on the relationship between sepsis, multiple organ dysfunction, and intestinal wall permeability. It has been revealed that systemic inflammation negatively affects the intestinal wall permeability, disrupting its protective barriers and inducing bacterial translocation. Therefore, bacterial cells from the intestines enter the circulating blood, thereby forming a "vicious circle." Moreover, Peng Chen et al. (2018) conducted an experiment with a group of mice that received fecal microbiotic transplantation (FMT) from patients with sepsis (main group) and compared it with a healthy group of mice (control group). As a result, it was revealed that the main group of mice had more inflammatory damage to the intestine with the subsequent formation of enteric eubiosis and their intestine became the

main root cause of sepsis and the formation of MODS, which once again proves the correlation between the activity of the intestinal wall permeability and the systemic inflammatory response with the formation of multiple organ dysfunction.

The main purpose of this review paper is to collect information regarding the relationship between intra-abdominal hypertension and markers of bacterial translocation, particularly, such markers as presepsin (s-CD-14), fatty acid binding protein (I-FABP), zonulin in critically ill patients.

Search strategy.

The search for papers was carried out on Pubmed, Scopus, Google Scholar and Web of Science platforms over the past 10 years (from 2013 to 2023). The search strategy included: [abdominal hypertension/OR intra-abdominal hypertension/AND presepsin/OR exp abdominal surgery/] AND [exp abdominal compartment syndrome/OR exp abdominal pressure/OR exp intraabdominal hypertension/OR intraabdominal pressure.mp OR abdominal compartment.mp OR exp intra-abdominal hypertension/or intra-abdominal pressure.mp] AND [risk*.mp OR predict*.mp] AND [abdominal hypertension/OR intra-abdominal hypertension/AND I-FABP /OR exp abdominal surgery/] AND [abdominal hypertension/OR intra-abdominal hypertension/AND multi organ disfunction /AND I-FABP /AND sCD14].

Inclusion criteria: all research papers that included patients with multiple organ dysfunction, abdominal hypertension, and surgical diseases of the gastrointestinal tract. Patients in intensive care units who underwent detection of bacterial translocation proteins, particularly, I-FABP, presepsin, and zonulin. In addition, experimental papers with animals using the same criteria over the past 10 years.

Exclusion criteria: studies that were published before 2013, as well as studies that did not have the main search criteria (abdominal hypertension, multiple organ dysfunction, markers of bacterial translocation were not detected). Patients under 18 years of age, patients with bladder injury or cancer.

Key requests: multiple organ dysfunction, abdominal hypertension, intra-abdominal hypertension syndrome, I-FABP, presepsin, zonulin, gastrointestinal diseases, sepsis, multiple organ failure.

Considering the uniqueness of the study, 154 papers were identified and selected according to the search strategy. Of the 154 papers, 88 related to the topic of this paper were reviewed on available platforms. A schematic search strategy is presented in Figure 1.

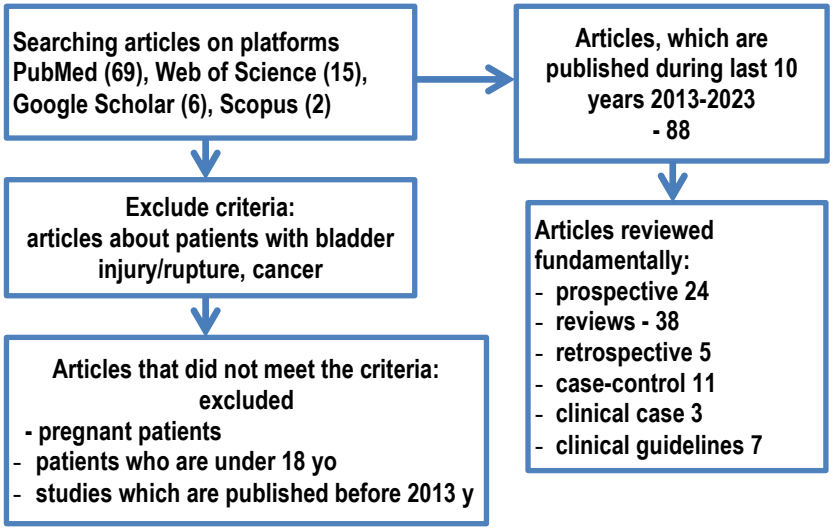

Figure 1. Search strategy.

Results and discussions

Relationship between IAH and bacterial translocation.

Based on clinical data, it is well known that intra-abdominal hypertension associated with surgical and therapeutic diseases is identified. It is proved that the level of IAH and the degree of progression of surgical or therapeutic complications do not have a clear correlation [12,13,14]. However, some studies have noted the identification of early markers of organ dysfunction, which makes them a necessary diagnostic tool [15,26]. A parallel increase in intra-abdominal hypertension and the level of biomarkers indicate organ injury at an early stage.

It is also known that after surgical treatment or injury, there is an increase in intra-abdominal hypertension and, as a result, damage to enterocytes and their strong bonds [16,29]. Further, toxins, bacteria, and undigested waste products can pass through the strong bond of the enterocytic barrier, which consists of a network of Tj proteins [34,78], penetrate into the vascular layer, and cause an inflammatory reaction, which is the onset of the process of multiple organ dysfunction that leads to death. Peptides that are released due to disruption of the enterocytic barrier and strong enterocytic bonds are ideal markers for identifying, due to early IAH, disruption of the intestinal barrier [17,18].

As a result of intestinal hypoperfusion due to increasing of intraabdominal pressure (more than 12 mm), ischemia of the mucous membrane and tissue acidosis appears and its barrier function is disrupted so, as a result, translocation of bacteria through the intestinal wall occurs with the generalization of the infectious process, also endotoxsins comes out, which provoke a cascade of cytokines into the blood from the intestinal lumen [20,21]. Translocation of bacteria from the ischemic intestinal

mucosa into the portal system and sepsis are a consequence of intra-abdominal hypertension.

That process in the case of intra-abdominal pressure of over 25 mmHg develops within one hour. Ischemia of the mucosa of the small intestine and portal hypertension developed in view of "compression" are the causes of edema of internal organs, which further increases the volume of the contents of the abdomen and thus aggravates the course of IAH [23,24], forming the so-called "vicious circle". Peptides (such as I-FABP, presepsin, etc.) that are released as a result of disruption of the integrity of the enterocyte under the influence of IAP are ideal biomarkers that help identify in a non-invasive way patients with early IAH and pathology of the gastrointestinal tract in patients in the intensive care unit.

Presepsin or sCD14 and gastrointestinal diseases.

To date, an early biomarker of bacterial translocation, which was discovered by Japanese scientists in 2005, presepsin or sCD14, is identified in the blood of patients even before the clinical manifestation of sepsis [25,85]. This is a glycoprotein weighing about 55 kDA, which is detected on the surface of monocytes, macrophages, neutrophils, and other myeloid cells. It also reacts in a timely manner with the effectiveness of therapy, which is an undoubted advantage in comparison with other diagnostic methods presented in the existing protocols [26,81].

One of the first studies in experimental conditions of the relationship between the level of the sCD-14 marker and the level of intra-abdominal pressure was carried out by D. N. Matyushko in his dissertation paper (2016). 10 groups of animals (rats) were formed, 1 control group + 9 experimental groups. In each group, the intra-abdominal pressure was artificially created by introducing gas through the abdominal wall using a needle, that is, pneumoperitoneum was created. Next, an exposure of 3-4 hours was ensured. Together with experts from the E.A. Buketov Institute, a special device to measure intra-abdominal pressure was created. In all animals from 10 groups, intra-abdominal pressure was invasively measured and blood was taken to identify the sCD-14 marker, among other things. As a result, it was found that in the control group, the level of presepsin was normal and in groups where pneumoperitoneum was created and intra-abdominal pressure was over 12 mmHg, presepsin (s-CD-14) was 7-10 times higher, which indicates of an immediate reaction of this marker in response to the release of gram-negative flora due to increased intestinal wall permeability [52,85].

Presepsin levels vary in healthy patients, SIRS (systemic inflammatory response syndrome) patients, and patients with diagnosed sepsis within the range of 258.7±92.53ng/L, 430.0±141.33ng/L, 1,508.3±866.6ng/L, respectively [48]. Studies published in leading journals have shown that the level of presepsin in the blood of patients with IAH of over 16 mmHg has a direct correlation and therefore, it is the main biomarker for the development of IAH and timely treatment of sepsis even before the development of the clinical picture [53,82]. According to studies, the level of the sCD14 marker increases depending on the level of IAH in patients with various surgical diseases. The paper by Mugazov M et al. (2019) presents a correlation diagram of the presepsin marker with groups of patients with IAH of grades 1-4. Groups were distributed according to the level of IAH, i.e. group 1 with IAP within the normal range of 0-4 mm Hg (control group), group 2 with IAP of 5-15 mmHg, group 3 with IAP of 16-25 mmHg, and group 4 with IAP of 26-35 mmHg [54,83,84].

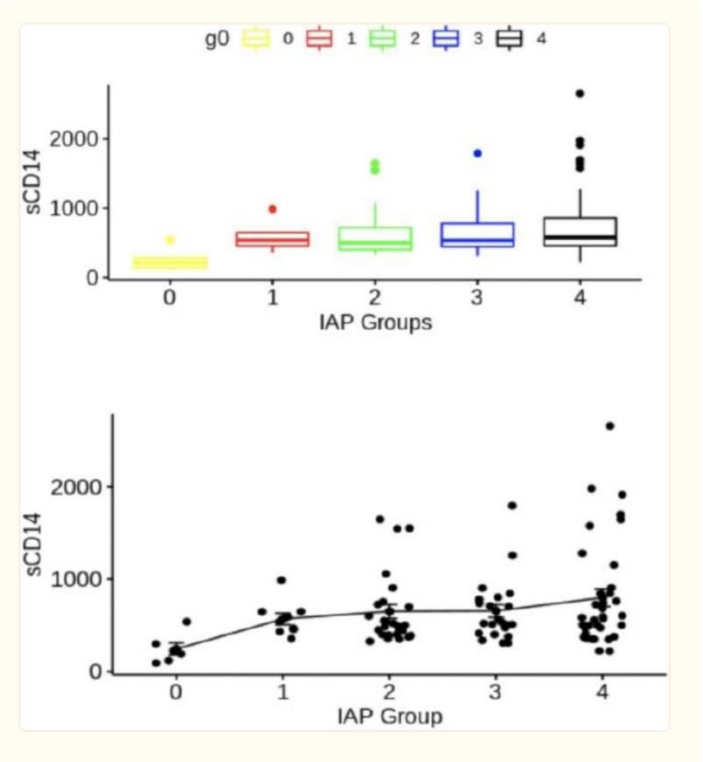

Figure 2. The influence of intra-abdominal hypertension on the course of acute surgical diseases of the abdominal organs (prospective clinical study). (Mugazov M. et al. (2019))

As a result, the average value of the macropresepsin in groups with IAP greater than 12 and under 35 mmHg increased from 246 to 800 pg/mL, respectively [55].

Fatty acid binding protein, intestinal form (I-FABP), and gastrointestinal diseases.

The highest levels of this protein were detected in critically ill patients in the ICU after surgical treatment - left-sided hemicolectomy; according to the authors, the cause was devascularization of the intestine during colectomy [61,62]. Moreover, an increase in I-FABP levels was observed in patients with irritable bowel syndrome (IBS) with diarrhea and in patients with strangulation obstruction of the small intestine, respectively. According to the authors, with a sensitivity of 100% and specificity of 83%, it can serve as a sign of necrosis of the small intestine [31,63].

Based on the published results, it can be concluded that there is a clear correlation between the level of I-FABP and the degree of intestinal ischemia or devascularization, as well as the inflammatory process.

According to the current data from the study, patients with abdominal trauma experience an increase in the level of fatty acid binding protein,

which in turn correlates as well with the level of hemorrhagic shock caused by the trauma. As part of the study, groups of patients with abdominal trauma and hemorrhagic shock, as well as patients without trauma but with shock, were created [64,65]. Subsequently, it turned out that in the group of patients without abdominal trauma but with hemorrhagic shock, the level of I-FABP increased dramatically on the first day of the disease. This suggests that fatty acid binding protein levels increase immediately in response to intestinal wall hypoperfusion [32,33]. The level of I-FABP is most sensitively detected in blood plasma by enzyme-linked immunosorbent assay (ELISA) [34,35].

According to the table (Table 1), in patients diagnosed with mesenteric thrombosis and gallbladder disease, as well as perforated gastric ulcer, the level of I-FABP is much higher than in patients from the control group [36,69,70].

Consequently, the researchers concluded that the determination of the I-FABP protein is a promising method for diagnosing diseases associated with the activation of bacterial intestinal translocation.

Table 1.

I-FABP level in various pathologies (Ozlem U. and ect 2014 y. Can Intestinal Fatty Acid Binding Protein (I-FABP) Be A Marker in the Diagnosis of Abdominal Pathology?)

Diseases	I-FABP level
Nonspecific abdominal pain ("acute abdomen")	53.5±55.7
Appendicitis	73.9±131.4
Gallbladder diseases	290.8±708.5
Colon diseases	130.8±221.9
Pancreatitis	112.1±167.1
Mesenteric thrombosis	708.6±669.1
Ovarian diseases	129.3±261.2
Gastritis, stomach ulcer	65.1±34.1
Urolithiasis, nephrolithiasis	40.7±32.1
Hernias	76.6±97.3
Perforated stomach ulcer and duodenal ulcer	438.1
Control group	61.4±47.4

Zonulin and gastrointestinal diseases.

Zonulin (the molecular weight of which is 50 kDa) is a protein that forms a network of Tj proteins located on the membrane of intestinal epithelial cells and consisting of two classes of proteins - claudins - sealing and vapor-forming, as well as other integral proteins. They form strong interepithelial bonds, which in turn limit intercellular transport [66,67,68]. Disruption of these protein complexes leads to destabilization of the intestinal wall permeability. The consequence of the above process leads to the penetration of pathogenic microorganisms, which stimulate the development of systemic inflammatory reactions and allergies, into the bloodstream. Zonulin is mainly detected in feces and blood. The detection of zonulin in the blood indicates the penetration of this protein from the intestinal lumen into the intercellular space of the intestinal epithelium and its detection in the feces indicates the rate of its production in enterocytes. A study conducted by G.P Caviglia et al. (2019) shows that it is more appropriate to identify the level of zonulin in the blood since a correlation was found between the level of zonulin and the duration of the disease, while in feces, there was no connection between the level of zonulin and the course of the disease [37,38]. Studies have shown that the level of zonulin in the blood when the intestinal wall permeability is impaired remains for 24 hours from the moment the process begins and it returns to normal after two days. However, given the fast half-life of the protein (up to 4 hours), researchers recommend detecting the presence of antibodies to it in the blood, i.e. IgG and IgM. In addition to enterocytes, zonulin is also secreted by cells of the liver, brain, lungs, kidneys, etc [73,74]. By regulating the intestinal wall permeability, zonulin helps wash out bacteria and intestines. An increase in zonulin levels has been recorded in diseases that impair intestinal barrier function, i.e. diabetes mellitus, celiac disease, Crohn's disease, oncology diseases, and surgery, respectively [39,40]. An increase in intra-abdominal pressure due to the development of various diseases, including surgical interventions, induces a violation of the intestinal barrier, which in turn precedes the development of inflammatory bowel diseases. The penetration of antigens from the intestine into the bloodstream stimulates the body's inflammatory immune response, which results in a violation of the intestinal wall permeability and therefore the so-called "vicious circle" is formed [41,42]. A study by *G.P Cavigla et al.* (2019) confirms the presence of a direct relationship between the level of zonulin and inflammatory bowel diseases (Crohn's disease, nonspecific ulcerative colitis, etc.). However, there are studies, in which the authors did not find a connection between zonulin levels and inflammatory bowel diseases induced by or without IAH. The authors explain this by the fact that the secretion of zonulin is possible not only by enterocytes but also by other cells [43,44]. The zonulin level in the study correlated with such criteria as body mass index, waist size, blood pressure, etc. Obesity occupies a special place among the criteria for increased zonulin levels. This relationship is currently being studied in clinical trials. It is known that, particularly, abdominal obesity causes increased intra-abdominal pressure and, as a consequence, impaired perfusion of the intestinal wall, which results in possible bacterial intestinal translocation [45,75]. It is assumed that the level of intestinal zonulin identified in the blood of patients with abdominal obesity and other metabolic disorders is a predictor of other related diseases associated with impaired intestinal wall permeability [76,77].

Conclusion.

Based on the analysis of papers and reviews in Pubmed, Scopus, and Web of Science publication databases, it can be argued that a few publications are devoted to the relationship between the level of markers of gastrointestinal injury and intra-abdominal hypertension in patients with multiple organ dysfunction. Recently, the relationship between the level of intra-abdominal hypertension and markers of bacterial translocation has been actively studied, which gives practitioners the opportunity to increase the number of clarifying non-invasive methods for diagnosing patients in intensive care units. The mortality rate of patients with diagnosed multiple organ dysfunction associated with increased abdominal pressure exceeds 80%, which proves the need for early diagnosis of immediate response markers, such as

presepsin, fatty acid binding proteins, and zonulin. Most studies reveal the need and benefit of blood testing for sCD-14 and I-FABP but results for zonulin proteins remain controversial, which suggests the need for further in-depth research.

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