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FORMATION OF INITIAL CHANGES IN HEMODYNAMICS AND FLUID COMPARTMENTS IN HIGH SURGICAL RISK PATIENTS UNDER THE INFLUENCE OF ACUTE ABDOMINAL PATHOLOGY

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Ключевые слова: *острая абдоминальная патология, дегидратация, объёмное истощение, водные секторы*

Abstract. Formation of initial changes in hemodynamics and fluid compartments in high surgical risk patients under the influence of acute abdominal pathology. Kravets O.V., Yekhalov V.V., Krishtafor D.A., Zozulia O.O., Volkov O.O., Vlasov O.O. *Among the main factors of pathological changes that accompany acute abdominal pathology are the inflammatory process of the peritoneum and fluid deficiency due to its pathological losses. The aim of our study was to analyze the initial state of fluid compartments of the body and hemodynamics in high surgical risk patients with acute surgical abdominal pathology. There were examined 157 patients with acute abdominal pathology who underwent emergency laparotomy. The presence and severity of fluid deficiency were determined clinically by tissue hydrophilicity test by P.I. Shelestiuk, biochemically – by assessing the levels of hematocrit, hemoglobin, erythrocytes, blood electrolytes, vasopressin (antidiuretic hormone (ADH)) and brain natriuretic propeptide (proBNP), as well as the mean erythrocyte volume and plasma osmolarity. Variables of fluid compartments of the body and central hemodynamics were studied using the non-invasive bioimpedancemetry. Based on the values of oxygen concentration in arterial and venous blood, total oxygen consumption (VO_2) and delivery of oxygen (DO_2), oxygen extraction ratio (O_2ER) were calculated. The detected changes indicate intravascular fluid deficiency and concomitant hemoconcentration with normal electrolytes levels and plasma osmolarity. In patients with high surgical risk and moderate dehydration according to P.I. Shelestiuk, urgent surgical pathology of the abdominal cavity reduces extracellular fluid volume by 19.1% (p=0.019) of the reference by reducing the volume of the interstitium and intravascular fluid respectively by 20.7% (p=0.002) and 16.3% (p=0.001) of regional values, which forms in patients a state of "volume depletion" of moderate severity. This is accompanied by an increase in the ADH concentration by 16.7% (p=0.041) above reference and normal proBNP levels. Stroke volume decreases by 28.8% (p=0.021) against tachycardia (increase in heart rate by 39.7% (p=0.001) above normal) and vascular spasm (increase in systemic vascular resistance by 86.9% (p=0.001) above reference), which supports the normodynamic type of blood circulation (cardiac index – 3.2 (0.4) $l/min/m^2$) with the decrease in stroke index and peripheral perfusion index by 41.3% (p=0.002) and 55.2% (p=0.002) from reference, respectively. DO_2 decreases by 11.1% (p=0.011) from reference with VO_2 increased by 16.3% (p=0.004) above reference, which leads to a decrease in oxygen utilization by 7.2% (p=0.041) from reference.*

Реферат. Формування вихідних змін гемодинаміки та водних секторів у пацієнтів високого хірургічного ризику під впливом гострої абдомінальної патології. Кравець О.В., Єхалов В.В., Кріштафор Д.А., Зозуля О.О., Волков О.О., Власов О.О. *Серед головних чинників патологічних змін, що супроводжують гостру абдомінальну патологію, виділяють запальний процес очеревини та дефіцит рідини внаслідок її патологічних втрат. Метою нашого дослідження було провести аналіз вихідного стану водних секторів організму та гемодинаміки в пацієнтів високого хірургічного ризику при гострій хірургічній абдомінальній патології. Було обстежено 157 пацієнтів з гострою абдомінальною патологією, які потребували екстреної лапаротомії. Наявність та ступінь дефіциту рідини визначалися клінічно за пробою на гідрофільність тканин за П.І. Шелестюком, лабораторно – за допомогою оцінки рівнів гематокриту, електролітів крові, вазопресину (антидіуретичного гормону (АДГ)) та мозкового натрійуретичного пропептиду (МНП), а також середнього об’єму еритроцита та осмолярності плазми. Методом неінвазивної біоімпедансометрії вивчали показники водних секторів організму та центральної гемодинаміки. На основі показників концентрації кисню в артеріальній та венозній крові розраховували загальне споживання (VO_2) та доставку кисню (DO_2), коефіцієнт екстракції кисню (O_2ER). Виявлені зміни свідчать про дефіцит внутрішньосудинної рідини та супутню гемоконцентрацію на тлі нормального вмісту електролітів* *та осмолярності плазми. У пацієнтів високого хірургічного ризику з 2 ступенем дегідратації за П. І. Шелестюком невідкладна хірургічна патологія органів черевної порожнини зменшує об'єм рідини позаклітинного простору на 19,1% (p=0,019) від норми за рахунок зниження об'ємів інтерстицію та внутрішньосудинної рідини відповідно на 20,7% (p=0,002) та 16,3% (p=0,001) від регіональних показників, що формує в пацієнтів стан «об'ємного виснаження» середнього ступеня тяжкості. Це супроводжується збільшенням концентрації АДГ на 16,7% (p=0,041) понад норму при нормальному рівні МНП. Ударний об'єм знижується на 28,8% (p=0,021) від норми на тлі тахікардії (збільшення ЧСС на 39,7% (p=0,001) понад норму) та судинного спазму (підвищення загального периферичного опору судин на 86,9% (p=0,001) понад контрольні показники), що підтримує нормодинамічний тип кровообігу (серцевий індекс – 3,2 (0,4) л/хв/м^2) на тлі зниження ударного та периферичного перфузійного індексів відповідно на 41,3% (p=0,002) та 55,2% (p=0,002) від норми. DO_2 знижується на 11,1% (p=0,011) від норми при підвищеному на 16,3% (p=0,004) понад норму VO_2, що призводить до зниження утилізації кисню на 7,2% (p=0,041) від норми.*

Acute abdominal pathology accounts for the majority of patients in surgical hospitals. It requires emergency surgery and is accompanied by a number of pathological changes in the body. Among the main pathological factors that form the corresponding changes are the inflammatory process of the peritoneum and fluid deficiency due to its pathological losses [2, 10]. Thes group of high surgical risk patients is independently increasing in the world, characterized by adverse treatment outcomes. According to the systematic reviews, age and baseline state severity, a significant influence on the short- and long-term mortality was established [3, 5, 9, 13, 15].

Aim of our study was to analyze the initial state of fluid compartments of the body and hemodynamics in high surgical risk patients with acute surgical abdominal pathology.

MATERIALS AND METHODS OF RESEARCH

There were examined 157 patients with acute abdominal pathology who underwent emergency surgery in the extent of emergency laparotomy. 80 (50.9%) were males, 77 (49.1%) – females. Mean age was 69.5 [60; 75] years.

The study was performed in accordance with the requirements for limited clinical trials of the Pharmacological Committee of the Ministry of Health of Ukraine, the Universal Declaration of Bioethics and Human Rights (1997), the European Convention on Human Rights and Biomedicine (1997), WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects (2000) as amended (2013), orders of the Ministry of Health of Ukraine No. 690 dated 23.09.2009, No. 944 dated 14.12.2009, No. 616 dated 03.08.2012.

Inclusion criteria: age from 45 to 75 years; urgent laparotomy; moderate dehydration according to P. I. Shelestiuk; high surgical risk on the P-POSSUM scale; informed consent to participate in the study.

Exclusion criteria: age under 45 and over 75 years; elective surgical interventions; mild or severe dehydration according to P. I. Shelestiuk; low or moderate surgical risk on the P-POSSUM scale [5]; gastrointestinal bleeding; multiorgan failure syndrome; intraoperative blood loss over 500 ml; secondary fibrinous-purulent or purulent peritonitis; total mesenteriothrombosis of the intestine; decompensated somatic pathology; oncological diseases regardless of location and stage; refusal of the patient to participate in the study.

The first group (n=57) consisted of retrospectively studied patients (R), the second group (n=100) patients were studied prospectively (P).

Detailed history was collected in all patients, and clinical, hardware, laboratory and calculation methods were used. The presence and severity of fluid deficiency were determined in all patients clinically – by assessing the dehydration severity with the tissue hydrophilicity test (THT) by P. I. Shelestiuk [2], biochemically – by assessing the levels of hematocrit (Ht), hemoglobin (Hb), erythrocytes (red blood cells (RBC)), blood sodium, potassium, chlorine and calcium (Na^+, K^+, Cl^- and Ca^{2+}), vasopressin (antidiuretic hormon (ADH)) and brain natriuretic propeptide (proBNP) and calculations of mean RBC volume (mean corpuscular volume, MCV, fl) and plasma osmolarity (Osm, mosm/l) with the respective formulas [2, 14].

All patients, according to the rules of propaedeutics of internal diseases, underwent a physical examination, which included determination of heart rate (HR), central venous pressure (CVP), systolic (SBP) and diastolic (DBP) blood pressure, followed by calculation of mean arterial pressure (MAP) according to the Hickem formula [12].

Body fluid compartments and the central hemodynamics were measured using non-invasive bioimpedancemetry monitoring complex of cardio-respiratory system and tissue hydration KM-AR-01 "Diamant" (Russia). Variables of body fluid compartments included: extracellular (ECFV, l), intracellular (ICFV, l) and intravascular fluid volumes (IVFV, l), plasma volume (PV, l) and total body fluid volume (TBFV, l). Based on the basic physiology of fluid distribution, interstitial fluid volume (ISFV, l) was calculated by the corresponding formula [14]. Cardiac output (CO), cardiac index (CI), stroke volume (SV), stroke index (SI), systemic vascular resistance (SVR), and peripheral perfusion index (PPI) were recorded. Hemodynamics type was determined according to CI values [12]. Total oxygen consumption (VO_2, ml/min), total oxygen delivery (DO_2, ml/min×m^2) and oxygen extraction ratio (O_2ER, %) were calculated by the applicable formulas [14].

To determine regional reference range, 40 assumedly healthy volunteers (mean age 60.3 (9.3) years) were examined. Their results were taken as the normal reference range.

Descriptive and analytical biostatistics methods were used for statistical processing of research materials. Statistical processing of the study results was performed using Microsoft Excel (Office Home Business, serial 2KB4Y-6H9DB-BM47K-749PV-PG3KT) and software pack STATISTICA 6.1 (StatSoftInc., serial AGAR909E415822FA) and included checking the quantitative data distribution to the distribution of Shapiro-Wilk, Kolmogorov-Smirnov and Lillefort. The obtained results were accounted using the methods of parametric and nonparametric biostatistics. Descriptive statistics of quantitative variables included: arithmetic mean (M), standard error (m), standard deviation (SD), 95% confidence interval (95% CI) in normal data distribution, and median (Me) and interquartile range (25%; 75%) for data with distribution other than normal. Correlation analysis was performed by calculating the Pearson linear correlation (r) and Spearman's rank correlation (rs) coefficients according to the conditions of their application [1].

RESULTS AND DISCUSSION

According to the P-POSSUM scale, all patients were at high surgical risk. The analysis of the obtained data established that the mean time from the disease onset to admission to the hospital was 1.7 (0.3) days. 80.3% (n=126) of patients were classified as American Society of Anesthesiologists (ASA) class III, 19.7% (n=31) – ASA class IV.

The morbidity structure was dominated by strangulated hernia in 47.2% (n=74) patients and acute intestinal obstruction – 36.9% (n=58) patients. Perforation of gastric or duodenal ulcers was diagnosed in 15.9% (n=25) of patients.

Analysis of peripheral blood count in high surgical risk patients (Table 1) showed a Hb increase by 7.8% (p=0.025), RBC – by 9.8% (p=0.017), Ht – by 7.1% (p=0.007) above reference. MCV decreased by 3.8% (p=0.033). These changes indicated intravascular fluid deficiency and concomitant hemoconcentration. The levels of blood serum Na^+, K^+, Ca^{2+}, Cl^- and plasma osmolarity did not differ statistically from the reference (p>0.05 for each variable). This indicated a simultaneous loss of fluid and electrolytes, which is inherent in the state of "volume depletion".

Table 1

Baseline values of peripheral blood count, electrolytes and plasma osmolarity in patients of subgroups P and R, M (SD)

Variable	Reference (n=40)	Subgroup R (n=57)	Subgroup P (n=50)	Total (n=157)	p	p_1
Hb, g/l	129.3 (8.7)	139.5 (5.1)	141.5 (4.9)	140.4 (5.0)	0.025	0.693
RBC, ×10^{12}/l	4.1 (0.3)	4.6 (0.2)	4.4 (0.1)	4.5 (0.1)	0.017	0.264
Ht, l/l	0.42 (0.01)	0.45 (0.01)	0.45 (0.01)	0.45 (0.01)	0.014	0.465
MCV, fl	98.3 (4.9)	95.3 (3.7)	93.3 (5.2)	94.6 (4.7)	0.033	0.588
Na^+, mmol/l	141.8 (1.8)	143.8 (0.2)	140.4 (0.2)	142.3 (0.3)	0.518	0.316
K^+, mmol/l	3.6 (0.1)	-	3.7 (0.1)	3.7 (0.1)	0.844	0.564
Ca^{2+}, mmol/l	1.23 (0.11)	-	1.23 (0.10)	1.23 (0.10)	0.742	0.321
Cl^-, mmol/l	102.5 (0.9)	98.8 (4.9)	100.6 (4.5)	98.9 (4.8)	0.532	0.519
Osmolarity, mosm/l	299.7 (2.5)	300.5 (1.4)	300.2 (1.4)	300.3 (1.2)	0.745	0.123

Notes: p – difference between the regional reference range and the main sample by Student's t test (t); p_1 – difference between groups by ANOVA one-way analysis of variance.

Indeed, the analysis of the initial body fluid compartments state (Table 2) found a decrease in ECFV by 19.1% (p=0.027) from the regional reference. This was due to a decrease in IVFV and ISFV by 16.3% (p=0.001) and by 20.7% (p=0.001), respectively. Intravascular deficiency fully correlated with PV deficiency and formed a negative correlation with serum Ca^{2+} levels (rs=-0.30, p =0.001). ICFV did not differ significantly (p=0.061) from the reference range. These changes were in line with a decrease in TBFV by 10.0% (p=0.002) from the reference and were accompanied by a reduction in THT time by 31.3% (p=0.019) in all patients. Thus, acute abdominal pathology causes fluid abnormalities, which are manifested by redistribution of the fluid compartments volume in the form of "volume depletion" in the absence of dehydration signs.

Table 2

Clinical and instrumental study of the baseline body fluid compartments in patients of subgroups R and P, M (SD)

Variable	Reference (n=40)	Subgroup R (n=57)	Subgroup P (n=50)	Total (n=157)	p	p_1
ECFV, l	14.1 (0.9)	-	11.4 (0.3)	11.4 (0.4)	0.027	0.966
ICFV, l	24.9 (1.7)	-	23.7 (0.5)	23.7 (0.6)	0.061	0.898
TBFV, l	39.0 (2.7)	-	35.1 (1.0)	35.1 (1.2)	0.002	0.961
PV, l	2.7 (0.2)	-	2.3 (0.1)	2.3 (0.1)	0.001	0.958
IVFV, l	4.9 (0.3)	-	4.1 (0.2)	4.1 (0.2)	0.001	0.877
ISFV, l	9.2 (0.6)	-	7.3 (0.4)	7.3 (0.4)	0.001	0.834
THT, min	>40.0	27.5 (1.4)	27.5 (1.5)	27.5 (1.5)	0.019	0.638

Notes: p – difference between the regional reference range and the main sample by Student's t test (t); p_1 – difference between groups by ANOVA one-way analysis of variance.

The above-described initial "volume depletion" was accompanied by an increase in ADH concentration by 16.7% (p=0.041) above reference (Table 3), which confirmed the extracellular fluid deficiency. A correlation was found between the ADH level and PV (rs=0.19, p<0.01). The concentration of proBNP did not differ statistically from the reference (p=0.941).

Table 3

Markers of baseline volume status of patients of subgroups R and P, Me (25%; 75%)

Variable	Reference (n=40)	Subgroup R (n=57)	Subgroup P (n=50)	Total selection (n=157)	p	p_1
proBNP, pmol/ml	63.8 (53.5; 78.4)	-	65.5 (56.4; 82.1)	65.5 (56.4; 82.1)	0.941	0.452
ADH, pg/ml	4.2 (4.0; 11.6)	-	4.5 (4.6; 7.2)	4.5 (4.6; 7.2)	0.041	0.543

Notes: p – difference between the regional reference range and the main sample by Mann-Whitney test (U); p_1 – difference between groups by ANOVA one-way analysis of variance.

As always, adaptive hemodynamic changes are formed in response to a decrease in IVFV. Manifestations and severity of hemodynamic adjustment depend on the rate and volume of fluid loss. Analysis of baseline central and peripheral hemodynamics (Table 4) found a decrease in SV by 28.8% (p=0.001) of reference, which was accompanied by an increase in SBP, DBP and MAP by 11.4% (p=0.037), 6.9% (p=0.049) and 24.9% (p=0.027) above reference, respectively. At the same time, CI decreased by 17.9% (p=0.032) from the regional reference range, but still met the criteria of normodynamic type of blood circulation. This was provided by an increase in HR by 39.7% (p=0.001) and in SVR – by 86.9% (p=0.001). Peripheral vasospasm was accompanied by a decrease in SI and PPI by 41.3% (p=0.002) and 55.2% (p=0.002) from reference, respectively, indicating abnormalities in peripheral blood circulation and systemic oxygen transport. Indeed, DO_2 decreased by 11.1% (p=0.011) from reference in the setting of increased oxygen consumption and reduced utilization. Thus, the VO_2 index exceeded reference range by 16.3% (p=0.004), while O_2ER decreased by 7.2% (p=0.041) from the reference.

Table 4

Baseline values of central and peripheral hemodynamics, oxygen metabolism in patients of subgroups R and P, M (SD)

Variable	Reference (n=40)	Subgroup R (n=57)	Subgroup P (n=50)	Total selection (n=157)	p	p_1
SBP, mm Hg	125.6 (7.7)	141.9 (9.3)	136.1 (6.8)	139.9 (6.7)	0.037	0.735
DBP, mm Hg	80.6 (6.9)	85.3 (5.8)	85.6 (4.1)	85.4 (6.9)	0.049	0.581
MAP, mm Hg	82.6 (2.9)	102.5 (4.9)	100.3 (5.0)	101.2 (3.7)	0.027	0.432
HR, bpm	76.3 (7.9)	103.0 (3.1)	108.1 2.8)	106.6 (4.3)	0.002	0.826
SV, ml	80.0 (6.8)	-	57.1 (7.9)	57.1 (7.9)	0.021	0.724
SI, ml/m^2	46.1 (2.5)	-	30.3 (4.1)	30.3 (4.1)	0.002	0.915
CO, l/min	6.1 (0.6)	-	7.6 (0.6)	7.6 (0.6)	0.017	0.743
CI, l/min/m^2	3.9 (0.3)	-	3.2 (0.1)	3.2 (0.1)	0.028	0.739
SVR, dyne×sec×cm^{-5}	1279 (156)	-	2417 (340)	2417 (340)	0.018	0.698
CVP, mm Hg	4.4 (1.6)	1.4 (0.1)	1.8 (0.2)	1.5 (0.2)	0.032	0.345
PPI, abs. units	2.5 (0.6)	-	1.3 (0.1)	1.3 (0.1)	0.002	0.934
DO_2, ml/min×m^2	664.2 (33.2)	-	589.8 (40.1)	589.8 (40.1)	0.011	0.723
VO_2, ml/min	180.0 (10.0)	-	209.8 (15.2)	209.8 (15.2)	0.002	0.871
O_2ER, %	30.0 (4.2)	-	28.1 (1.9)	28.1 (1.9)	0.041	0.965

Notes. p – difference between the regional reference range and the main sample by Student's t test (t); p_1 – difference between groups by ANOVA one-way analysis of variance.

Development of the inflammatory process in the abdominal cavity is accompanied by a disruption of the body fluid and electrolyte balance, and is confounded by pathological fluid loss. In clinical practice, fluid deficiency in acute abdominal pathology is traditionally characterized as "dehydration" [2, 6, 8, 11]. However, dehydration is loss of water without electrolytes, which causes the transfer of fluid from the cell into the extracellular space and forms an intracellular fluid deficit in a setting of plasma hyperosmolarity [4]. In our study, in high surgical risk patients with acute abdominal pathology, we did not find any baseline abnormalities of both plasma electrolyte levels (Na^+, K^+, Ca^{2+}, Cl^-) and its osmolarity, which doesn't meet the definition of dehydration [2, 6, 8, 11]. Intracellular fluid volume also didn't differ significantly from the reference, while the extracellular fluid volume decreased due to both circulating blood volume and interstitial fluid volume deficiency. These changes were consistent with a decrease in TBFV by 10.0% (p=0.002) from the regional reference and were accompanied by a reduction in THT time by 31.3% (p=0.019) in all patients. Thus, acute abdominal pathology in high surgical risk patients with moderate dehydration according to P. I. Shelestiuk is accompanied by the loss of both water and electrolytes, which keeps the plasma isoosmolar. Such a deficit of body fluid is understood as a "volume depletion", a decrease in the extracellular fluid volume, which forms a deficit of both intravascular ("intravascular depletion") and interstitial fluid volumes [4, 7]. We believe that it makes sense to further develop the study of baseline changes in water-electrolyte status and body fluid compartments in patients with acute abdominal pathology of varying severity.

Changes in cardiovascular function were due to the formation of hypovolemia and corresponded to the slow rate of fluid loss, which does not contradict the generally accepted postulates [4, 7].

CONCLUSIONS

In patients with high surgical risk and moderate dehydration according to P. I. Shelestiuk, urgent surgical pathology of the abdominal cavity:

1. reduces extracellular fluid volume by 19.1% (p=0.019) of the reference due to the reduction of interstitial fluid volume and intravascular fluid volume by 20.7% (p=0.002) and 16.3% (p=0.001), respectively, and forms a state of "volume depletion" of moderate severity in patients;
2. reduces stroke volume by 28.8% (p=0.021) from reference against tachycardia (increase in heart rate by 39.7% (p=0.001) above reference) and vascular spasm (increase in systemic vascular resistanceby 86.9% (p=0.001) above reference);
3. supports the normodynamic type of blood circulation (cardiac index – 3.2 (0.4) l/min/m^2) in the setting of a stroke index, peripheral perfusion index and total oxygen delivery decrease by 41.3% (p=0.002), 55.2% (p=0.002), and 11.1% (p=0.011) of the reference, respectively, with increased oxygen consumption (increase in total oxygen consumption by 16.3% (p=0.004) above reference) and reduced utilization (decrease in oxygen extraction ratio by 7.2% (p=0.041) from reference).

Conflict of interests. The authors declare no conflict of interest.

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