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PEDIATRIC SURGICAL SEPSIS: DIAGNOSTICS AND INTENSIVE THERAPY

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The aim: Optimization of diagnostics and schemes of pathogenetic intensive therapy of surgical sepsis in children based on clinical and laboratory criteria and bacteriological monitoring.

Materials and methods: The research period is 2018-2020. The object of the study (n=73) – children with surgical pathology (widespread peritonitis, bacterial destruction of the lungs, post-traumatic brain hematomas, abdominal trauma, etc.). Research methods: microbiological monitoring to determine the sensitivity of the microorganism to antibiotics was carried out before and at the stages of treatment (sputum, urine, wound, bronchoalveolar lavage, tracheal aspirate, blood, contents from drainages, wound surface). Determination of the sensitivity of the isolated strains to antibiotics was carried out by the disk-diffusion method. To determine predictors of sepsis in surgical patients, clinical (mean arterial pressure (mAP), heart rate (HR), respiratory rate (RR), SpO₂, etc. and laboratory parameters on days 1–2 (up to 48 hours) of sepsis identification, days 4 and 8 of intensive therapy. Procalcitonin was determined by immunofluorescence on a Triage® MeterPro analyzer (Biosite Diagnostics, USA). Blood gases and electrolytes were analyzed using a Stat Profile CCX analyzer (Nova Biomedical, USA).

Results: studies have shown the effectiveness of complex intensive care in 86.3 % of cases. Mortality was found in 13.7 % of cases. Patients with severe surgical pathology died: widespread peritonitis, severe TBI + coma with irreversible neurological disorders, urosepsis against the background of chronic renal failure, after repeated surgical interventions, due to the development of refractory septic shock (SS).

Conclusions. Early diagnosis of sepsis, rational early ABT under the control of microbiological monitoring, non-aggressive infusion therapy with early prescription of vasopressors (SS) with constant monitoring of the child's main life support organs contribute to an improvement in sepsis outcomes and a decrease in mortality

Keywords: pediatric sepsis, balanced crystalloids, respiratory support, septic shock

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1. Introduction

Sepsis, as a life-threatening problem in modern medicine, has been repeatedly revised by the international medical community over the past 3 decades (Sepsis-1-Sepsis-2-Sepsis-3), definitions, approaches to early diagnosis and intensive care have changed, also changed rating scales of severity and prognosis of sepsis. The results of recent studies show that the information value of the criteria for systemic inflammatory response syndrome (IRS) is very low [1, 2]. It is proved that the very process of interaction of micro- and macroorganisms is more complex and is characterized by the versatility of the reaction of the latter to microbial invasion, the manifestations of which determine gender, age, race, genetic factors and concomitant pathology [1, 2]. As a result, sepsis has been defined as life-threatening organ dysfunction (OD) resulting from dysregulation of the host's response to infection.

All changes in the diagnosis and treatment of sepsis affected mainly adult patients and, to a lesser extent, children. It is important that among the highlighted pedi-

atric aspects of sepsis treatment there are no recommendations that are not classified according to the degree of evidence [3].

A multicenter study of sepsis in children (n=6925, SPROUT, 2014), conducted in 26 countries (in 128 pediatric intensive care units), revealed a significant variability in the incidence of sepsis from 6.2 % in Europe to 23.1 % in Africa, in the United States on average – 8.2 % [4]. On average, mortality from sepsis was 24 %. The most frequent foci of infection were the respiratory system (40 %) and blood flow (19 %) [5–7]. A detailed review of the epidemiology and geography of sepsis (2019) showed that in countries with a high level of economy, the incidence of sepsis varied widely from 1.4 % (Japan) to 7.7 % (USA), mortality from sepsis was 7–17 %. %, from the septic shock (SS) - 51 %. In small economies, the incidence of severe sepsis in children was 1–26 %, and the mortality rate was 12–35 %. The authors associate these significant fluctuations with various diagnostic criteria for sepsis and economic factors [8, 9]. Also, after discharge from the hospital, a fifth of the surviv-

ing children with sepsis were found to have moderate functional disability [10].

Thus, the need for early diagnosis and treatment of sepsis in children is confirmed by the continuing high rates of morbidity and mortality. To facilitate the diagnosis of sepsis in children, the pSOFA and PELOD-2 children's scales have been developed in recent years. They do not have 100 % specificity, but their use will help in the early diagnosis of sepsis [10, 11]. The authors of [12, 13] observed a very high predictive accuracy of these scales.

As a result of the selection of literary sources collected in the Pub Med, Science Direct, Cochrane Library databases, with a search depth of 10 years (2009–2019), 36 articles were selected on the problem under study. The number of controlled clinical trials of childhood sepsis is very small (with the exception of neonatal sepsis), and they all reflect an unsolved problem, a lack of a single concept and protocols for diagnosis and treatment.

The aim of the research. Optimization of diagnostics and schemes of pathogenetic intensive therapy of surgical sepsis in children based on clinical and laboratory criteria and bacteriological monitoring.

2. Materials and methods

A prospective, non-randomized case-control study. Research period 2018-2020 The inclusion criteria for patients in the study were signs of organ dysfunction (2+), procalcitonin >0.5 ng/ml, pSOFA>3 points, age – children under 18 years of age and the presence of the required examination volume. The exclusion criterion is the disagreement of the patient or his relatives to participate in the study. The study included 73 patients who underwent interventions for intestinal obstruction – 14, generalized peritonitis – 15, traumatic rupture of the intestine – 8 and esophagus – 1, bacterial destruction of the lungs – 6, wound infection – 3; craniocerebral trauma (subdural, intracerebral hematomas) – 11; congenital anomalies of the urinary tract, ureterohydronephrosis (2–4 degrees, chronic renal failure, urosepsis) – 15. The age composition of patients: preschoolers 2–5 years – 11, schoolchildren 6–12 years old – 44, adolescents 13–18 years old – 18 Schoolchildren prevailed and accounted for 60.3 % in the general structure of patients.

During the study, permission was obtained from all parents of patients in accordance with the code of ethics (2013). Approved by the conclusion of the expert commission of the ethical committee of the clinic of the Tashkent Pediatric Medical Institute of the Ministry of Health of the Republic of Uzbekistan (No. 475 of 21.10.2021). Artificial lung ventilation (ventilators SAV-INA, SULLA) lasting more than 48 hours was performed in 27 patients (36.9 %), of which nosocomial pneumonia was detected in 19 children (70.3 %). The length of stay in the intensive care unit averaged 19.3±5.6 days.

Microbiological monitoring to determine the sensitivity of the microorganism to antibiotics was carried out before and at the stages of treatment (sputum, urine, wound, bronchoalveolar lavage, tracheal aspirate, blood, contents from drains, wound surface). Determination of the sensitivity of the isolated strains to antibiotics was carried out by the disk-diffusion method. The results of microbiological monitoring are presented in diagrams 1,2,3,4.

To determine predictors of sepsis in surgical patients, we analyzed the clinical (mean arterial pressure (mAP), heart rate (HR), respiratory rate (RR), blood oxygen saturation (SpO₂), and laboratory parameters on day 1–2 (up to 48 hours) detection of sepsis, 4 and 8 days of intensive care. Thrombocytopenia was diagnosed with a platelet count <120,000/μL of blood, immunoglobulinemia G – with a serum level <7 g/L. Assessment of the state of the immune system was carried out based on a quantitative determination of the concentration of serum immunoglobulins IgG by flow cytometry. A Mindray BA-88A automatic biochemical analyzer was used to study AST, total protein, albumin, creatinine, and blood sugar. Procalcitonin was determined by the immunofluorescence method using a Triage® MeterPro analyzer (Biosite Diagnostics, USA). Blood gases and electrolytes were analyzed using a Stat Profile CCX analyzer (Nova Biomedical, USA). The results of clinical and laboratory studies are presented in Table 1. At all stages of intensive care, monitoring of the parameters RR, HR, BP, SpO₂, T body (Nihon Kohden) was carried out. Statistical data processing was performed using the Statistica 6.1 statistical software package (StatSoft, USA, 2003). Comparison of independent groups for quantitative characteristics was carried out using the Mann-Whitney U-test, qualitative comparison of independent groups - by analyzing contingency tables using the two-sided Fisher's exact test for unrelated groups or the χ^2 method with Yates' correction depending on the expected frequencies of the function.

3. Results

The diagnosis of sepsis was based on clinical and laboratory data and confirmed by identification of the pathogen culture in blood and / or other biosubstrates. Sowing of the same culture of the pathogen in 2 or more loci was bacteriologically confirmed by sepsis and was etiologically proven. Objective indicators of organ dysfunction were taken into account (100 % of cases). As noted above, sepsis is a heterogeneous process with pronounced individual variability, which complicates its diagnosis and treatment [14–17]. When making a diagnosis, the most important thing is the clinical picture of the disease. However, it is no less important for practicing physicians to monitor indicators of metabolism, hemodynamics, blood circulation and biomarkers of sepsis [18].

Patients who developed sepsis had severe hypermetabolic syndrome, which was manifested by tachycardia and tachypnea, hyperthermia, low levels of albumin and total protein in the blood. Among them, on the 2nd day (stage 1), hypoglobulinemia G and thrombocytopenia were more common (Table 1). Protein catabolism in patients was accompanied by a decrease in the synthesis of globulins (IgG) and the development of a secondary immunodeficiency state. There was a moderate increase in the level of fibrinogen, which characterizes the severity of the syndrome of disseminated intravascular coagulation, against the background of an inflammatory reaction with damage to microvessels, hemoconcentration, endothelial disorders, etc.

Table 1

Clinical, biochemical and special markers of sepsis in children (n=73, M±m)

Index	1–2 nd day (48 h)	4 th day	8 th day
MAP, mm Hg	84.5±4.3	80±4.8	72±3.5*^
Heart rate, min	129.4±7.2	118.6±5.7	107±5.1*^
Breathing rate, min ⁻¹	34.2±3.4	29.1±3.2	25.3±2.7*
Body temperature, °C	37.9±2.0	37.5±1.8	37.0±1.4
SpO ₂ , %	96±4.9	97±4.7	98±3.9
Leukocytes, 10 ⁹ /l	15.8±5.3	12.8±2.4	9.05±1.7**
Neutrophils, %	81.6±2.9	78.9±2.8	70.6±2.4**
Hemoglobin, g / l	105±5.6	114±4.3	117±3.8*
Platelets, 10 ⁹ /l	120.5±6.1	124.3±7.5	140.2±5.5*
Fibrinogen, g / l	5.1±1.2	4.8±1.3	4.0±1.4
Bicarbonate, mmol / l	23.2±2.5	22.8±2.1	22.1±2.4
AST, u / l	1.9±0.40	1.0±0.36	0.8±0.32*
Total protein, g / l	48.4±7.5	49.9±6.7	58.0±6.8*
Albumin, g / l	27.2±3.9	28.9±4.5	31.0±4.2
Creatinine, μmol / l	97.5±5.5	89.9±4.9	87.5±3.8*
Glucose, mmol / l	7.1±0.2	7.0±0.1	6.5±0.2
Ig G, g / l	6.01±1.7	6.58±1.9	7.0±1.8
C-reactive protein, mg / l	34.0±3.9	27.0±3.7	15.0±1.9**^
Procalcitonin, ng / ml	2.60±0.3	2.10±0.7	1.8±0.2*
pSOFA, points	9 ±2.5	7±1.6	4±0.9

Note: reliability of data on indicators for 1–2 days; * – $p < 0.05$; ** – $p < 0.01$; ^ – reliability of data to indicators on the 4th day, ^ – $p < 0.05$

Blood culture – a specific and affordable method – has always been considered the “gold standard” for diagnosing infection, but its sensitivity does not exceed 25–42 %. In addition, due to the use of antibiotics before blood sampling, blood cultures are often false negative. The causative agent remains unknown in 30–75 % of children with sepsis [20].

Blood sampling for bacteriological examination was carried out before the start of antimicrobial treatment. In most patients, blood samples and biomaterials from other loci were taken for bacteriological examination 2–3 times during their stay in the intensive care unit. The largest number of isolates was isolated from tracheal aspirate (sputum) – 39.7 %, surgical drains – 32.8 %, urine – 27.3 %, and blood – 26 %.

We followed the standard of testing blood for sterility from two peripheral veins at intervals of up to 30 minutes in two vials. Blood sampling from a central venous catheter was performed on the condition that it had just been inserted. To diagnose or exclude catheter-associated sepsis, blood sampling from a previously inserted catheter was allowed.

Bacteriological examination from different loci revealed the following data: from blood (Fig. 1) – staphylococcus, coagulase-negative – 42.5 % (8), St Aureus – 26.3 % (5), Streptococcus viridans et pneumoniae – 10.5 % (2), Enterococcus faecium – 5.4 %, Kl pneumoniae – 10.5 %, Pseudomonas spp. – 5.4 %. Gram-positive bacteria predominated: Staphylococcus, coagulase negative, and St aureus.

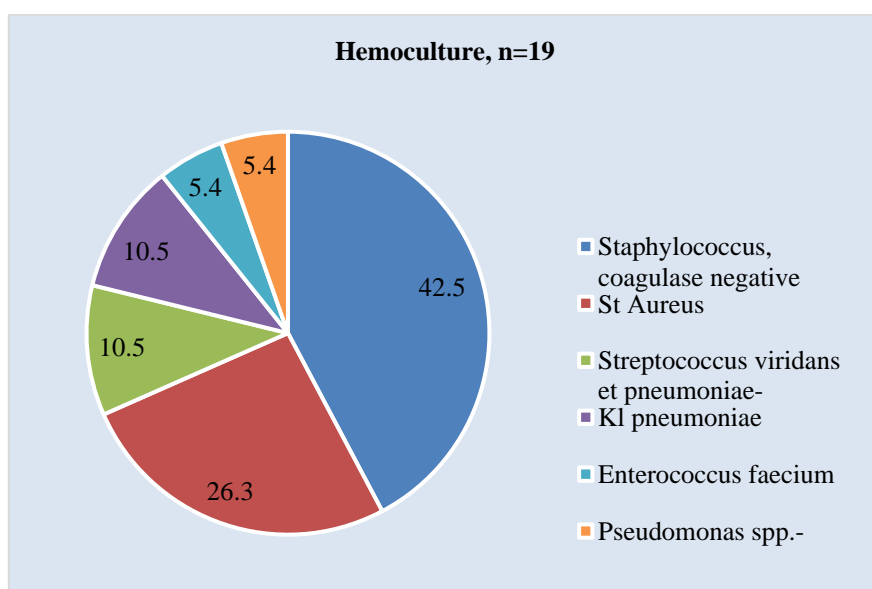


Fig. 1. Microbiological monitoring of blood culture

In turn, from surgical drains, peritoneal fluid, cerebrospinal fluid (Fig. 2) was sown in 29.1 % of cases (7) – *Kl pneumoniae*, in 25 % (6) – *Pseudomonas Aeruginosa*, in 16.6 % (4) – *St. Aureus*, in 20.2 % (5) – *Acinetobacter*, in 8.3 % (2) – *Enterobacteriaceae*.

From bronchoalveolar aspirate (Fig. 3) – *Kl. pneumoniae* – 27.5 % (8), *Ps. Aeruginosa* – 24.1 % (7), *St. Aureus* – 20.6 % (6), *Pneumococcus* – 17.2 % (5), *Acinetobacter* – 10.3 % (4) was obtained.

All over the world, multi-resistant superbugs, representatives of the ESCAPE group (*Enterococcus Faecium*, *St. aureus*, *Kl. Pneumonia*, *Acinetobacter*, *Ps.aeruginosa*, *Enterobacter spp.*), Pose a particular problem. Local monitoring confirmed the dominant position in the structure of the studied isolates of bacteria

such as *St. aureus et epidermidis*, *Ps. aeruginosa*, *Kl. pneumoniae* and *Acinetobacter*. In our study, *Kl. pneumoniae* exceeded *Ps.aeruginosa*.

Thus, the analysis of changes in the bacteriological landscape showed that the proportion of gram-negative microflora among the studied isolates remains consistently high. Fungi of the genus *Candida* were sown in 12.5 % of cases and were part of the polymicrobial flora. In general, when summarizing the results of other biological media of the patient, representatives of gram-negative flora (*Enterobacteriaceae*, *Pseudomonas*, *Kl.pneumoniae*) were the main causative agents of sepsis in 47.6 % of cases, gram-positive (*St. Aureus et epidermidis*, *Enterococcus*, *Pneumococcus*) – in 30 %, polymicrobial – in 21.8 % (Fig. 4).

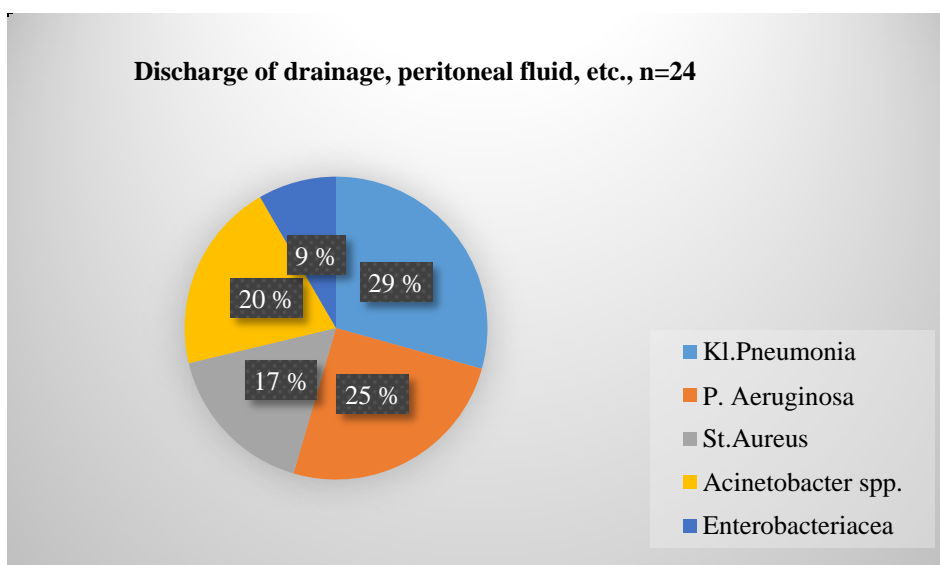


Fig. 2. Microbiological monitoring of peritoneal fluid and drains

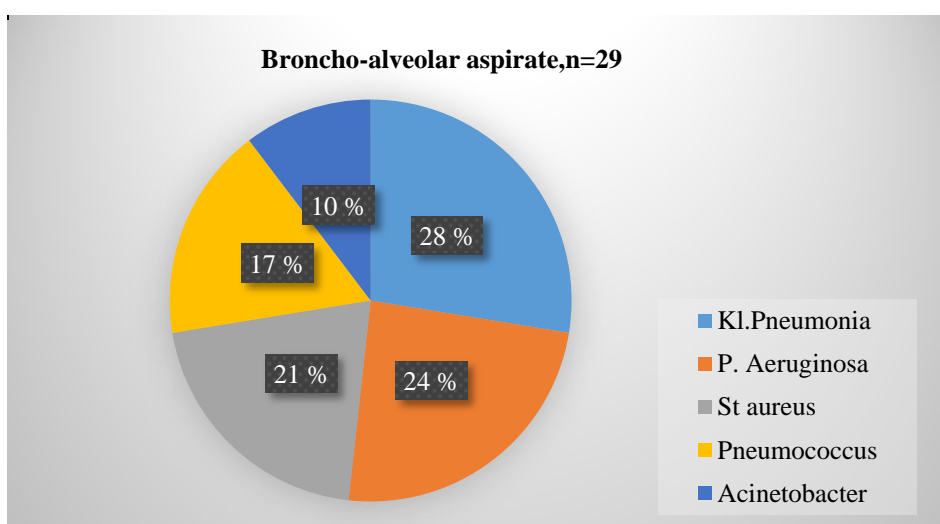


Fig. 3. Microbiological monitoring of broncho-alveolar aspirate

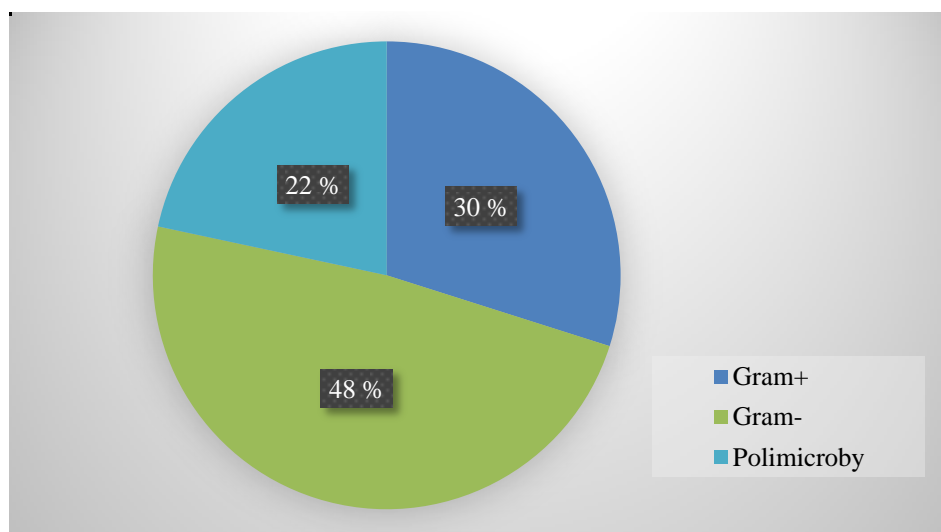


Fig. 4. The main causative agents of sepsis

Multicomponent intensive therapy for sepsis included detoxification therapy, respiratory support (if necessary, mechanical ventilation), correction of water-electrolyte, hemodynamic disorders, inotropic support, nutritional and immunotherapy.

Intensive therapy for sepsis / SS (the main provisions of the local protocol. Syndromic therapy of organ dysfunction was performed in all patients with sepsis / SS:

1. Respiratory support, mechanical ventilation (in 36.9 % of cases). Ventilation was carried out in controlled pressure (CP) mode with a quick transition to auxiliary ventilation modes. Gas exchange was monitored by KOS and blood gases, SpO_2 – 90–95 %.

CP, PRESSURE CONTROL SYSTEM. The leading controlled variable is inspiratory pressure (P_{insp}). Optional-f, PEEP. Initial installation parameters: P_{insp} <28 cm of water gauge; PEEP – 5–8 cm of water gauge (prevention of electrical injury); inspiration time 0.8 s (physiological); BH (f) – 20 (children >5 years old); FiO_2 – 0.8 (ideally 0.5–0.6)

2. Infusion-transfusion therapy. The calculation of infusion therapy for sepsis averaged 4–6 (4+2) ml/kg/hour with compensation for current losses. The qualitative composition of IT was represented by balanced crystalloids (Ringer's lactate solution), less often 0.9 % sodium chloride solution, as well as colloids (albumin) until mBP reached ≥ 60 mmHg, CVP – 8 mm Hg. In liquid refractory shock, when after intravenous administration of 2 boluses of 20 ml/kg of fluid (40 ml/kg) for 1 hour, A/D remains below the age norm, vasopressor support (dopamine, dobutamine, adrenaline, norepinephrine) was started, which depended on the type of septic shock. In hyperdynamic shock, norepinephrine was administered at a dose of 0.05–0.1 $\mu\text{g}/\text{kg}/\text{min}$. Epinephrine (0.05–0.2 $\mu\text{g}/\text{kg}/\text{min}$) replaced dopamine in children with hypodynamic shock. Dobutamine was prescribed to patients with low cardiac output and high vascular resistance (cold extremities, delayed capillary filling, decreased urine output after IT at normal blood pressure). Later, when the condition stabilized, the child received a physiological daily need for fluid, if necessary, against the background of diuretic therapy. Transfused with hemoglobin 70–90 g/l, erythro-

cyte mass. For fibrinolytic bleeding, fresh frozen plasma was transfused at a dose of 15 ml/kg.

3. Hormone therapy SS. Steroids for the treatment of refractory shock to infusion and vasopressor therapy. Children with resistance to catecholamines, with suspected adrenal insufficiency, were treated with hydrocortisone 1–2 mg/kg/day intravenously, then 150–250 mg for 3–4 injections.

4. Antibiotic therapy. Broad-spectrum antibiotics were prescribed within 2–3 hours of the diagnosis of sepsis. Considering the severity of the patient's condition caused by the septic process, the initial antibiotic therapy included 2 broad-spectrum antibiotics (3rd and 4th generation cephalosporins, 3rd generation aminoglycosides), often in conjunction with metronidazole. Protected beta-lactam antibiotics took precedence. The revision of the ABT scheme was carried out after receiving the results of a microbiological study (after 48–72 hours) and evaluating the clinical data in order to narrow the antibacterial spectrum to an adequate one (the principle of de-escalation).

So, in gram-negative sepsis, a deescalation mode of etiotropic ABT with protected CPs of 3-4 generations in combination with AH of the 3rd generation was used, then, if necessary, and according to microbiological monitoring data, the course of ABT was changed in extremely severe cases – carbapenems (KB, imipenem, meropenem), fosfomycin, fluoroquinolones 3–4 generations (reserve) in combination with other antibacterial drugs. The reasons for transferring patients to fluoroquinolones were: lack of effect from the previous ABT; high sensitivity of pathogens to them [20–22]. As a result of the study, a high resistance of KI was revealed. pneumoniae to cephalosporins 3–4, KB and even fluoroquinolones. For multi-resistant gram-negative flora, Polymyxin E (sodium colistimethate) was prescribed. It is used at a dose of 3–5 mg/kg/s every 8 hours intravenously (1 mg – 12500 IU) to patients without renal pathology (2/3 of the unchanged state is excreted by the kidneys during the day).

In the case of gram-positive sepsis, the emphasis was placed on the use of antibiotics from the groups of oxazolidinones and glycopeptides. In the presence of methicillin-resistant *S. aureus* (MRSA), coagulase-

negative staphylococcus, glycopeptides (vancomycin, teicoplanin) were used, and in the case of vancomycin-resistant strains – linolid. According to indications, anti-fungal drugs (fluconazole) were included in the ABT regimen for no more than 5 days.

The duration of antimicrobial therapy for sepsis averaged 16 ± 4.5 days. Patients with sepsis received from 1 to 5 courses of ABT, one course for 8–10 days.

5. Nutritional support (NS). The choice of NS method depended on the severity of nutritional status and gastrointestinal dysfunction. Patients with sepsis were given parenteral nutrition (PN) when full enteral nutrition was not available. The regime of round-the-clock administration of nutrients was observed, which is associated with better tolerance and metabolism. An early meal was prescribed – within 48 hours. Nutritional support: energy value of food -25-30 kcal / kg of body weight per day; protein – 1.5–2.0 g/kg/day; glucose – 30–70 % of non-protein calories while maintaining glycemic levels below 6.1 mmol/l; lipids – 15–20 % of non-protein calories. Glutamine 0.5 ml/min for 2 hours, 1.5–2 ml/kg/day for 5 days, infusion rate: 0.5 ml/min. Priority of enteral nutrition (glucose+IV). Contraindications to any nutritional support were refractory shock (arterial hypotension on the background of infusion of epinephrine or norepinephrine at a dose of more than 0.1 $\mu\text{g}/\text{kg}/\text{min}$); decompensated metabolic acidosis.

6. Immune replacement therapy. The results of the use of intravenous immunoglobulin G (IVIG, Biovena) at a dose of 0.4 g/kg/day from the 4th day of illness showed a relative stabilization of the clinical and laboratory manifestations of sepsis and the cessation of the decrease in globulins (IgG) by the beginning of the 2nd week of illness. IVIG was administered for 5 days against the background of complex pathogenetic intensive therapy for sepsis.

As can be seen from Table 1, against the background of the application of this protocol, there was a relative stabilization of clinical and biochemical parameters by 4 days of intensive care, HR and RR decreased by 8.4 % and 15 %, blood leukocytes by 19 %, procalcitonin and CR-protein by 19.3 % and 21 % respectively. After 2 weeks of complex intensive therapy, a significant stabilization of many of the studied parameters of homeostasis was noted. Procalcitonin and CR-protein at the 3rd stage of the study decreased by 30.8 and 55.9 % in relation to the initial data of the 1st stage. According to the results of pSOFA assessment in patients with sepsis, a tendency towards a decrease in signs of organo-systemic damage from stages 1 to 3 was revealed: 9 points – 7 points – 4 points, respectively. Procalcitonin correlated with the severity of the patient's condition on the pSOFA scale. In 10 patients, despite the ongoing complex treatment, the PCT index remained stable.

Clinical case

Patient – girl A., 1 year 2 months. (Fig. 5). Date of entry 12.08.19, Complaints (according to the mother): hyperthermia, lack of appetite, anxiety, shortness of breath, groaning breathing. Anamnesis: Illness for 10 days. In September 2019, she underwent inpatient treatment for pneumonia. In November she received a prophylactic vaccination against pneumococcal infection + against measles, rubella and mumps. From 01.12.19 the

condition worsened. Anxiety, fever, shortness of breath, refusal to eat, weakness, and abdominal pain appeared. Objectively: the general condition is severe, multiple organ dysfunction: acute respiratory failure of the 2nd degree, acute cardiovascular failure of stage 2B, acute cerebral failure, toxic encephalopathy. The child is lethargic. The skin and visible mucous membranes are sharply pale, bluish, dry. Breathing moans rapidly with the participation of accessory muscles. In the lungs on the right, hard wire breathing with dry wheezing. On the left, breathing is weakened. Deaf heart sounds, tachycardia. The abdomen is enlarged, swollen. Liver + 3.5 cm. There was no defecation for 2 days. Oliguria.

Ultrasound of the heart from 12/08/2019 – Pericardial effusion: an increase in the amount of fluid in the pericardium over the entire surface by 21-23 mm. Fibrin deposits. Ultrasound of the pleural cavity from 08.12.2019: free fluid is determined in the pleural cavities: On the right, 20.0 ml. There is still 80.0 ml. Clinical and biochemical analyzes (selectively): Hb 77 g/l; Leukocytosis – $11,8 \times 10^9/\text{l}$, Neutrophils 86 %, ESR – 18 mm/h. Medium molecules – 0.758 units. Total protein – 47.8 g/l. Urea – 18.2 mmol/l; AST – 4.8. Procalcitonin – 17 ng/ml, CRP – 42 mg/l. In urine, blood and throat: *St. aureus*, *Ps. Aeruginosa*.



Fig. 5. X-ray picture lung -12.08.2019. Hydrothorax from the left. Pericarditis

The clinical diagnosis was made:

Main: Bacterial destruction of the lungs, pulmonary-pleural-mediastinal form.

Complications: Hospital sepsis (Gr + and Gr-). Multiple organ dysfunction. Pyothorax on the left, purulent pericarditis. Toxic hepatitis-nephritis (hepato-renal syndrome). DIC syndrome. Encephalopathy.

On 10.12.19 the operation was performed for health reasons: sternotomy, pericardiotomy. Anterior pericardiectomy. Sanitation and drainage of the cavity. Purulent effusion in a volume of 100.0 ml.

Thoracocentesis 12/10/19: from the left pleural cavity through the drainage allocated 110.0 ml of purulent effusion. The drain is connected to active aspiration.

Intensive care: 1 course of ABT Cefoperazone + sulbactam + Vancomycin, 2 course – Meropenem + Anzolid (Oxazolidinone group). Infusion-transfusion therapy (Ringer, saline, albumin, washed erythrocytes).

Immunosubstitution therapy (Intravenous native immunoglobulins G (IVIG, Bioven) 0.4 g/kg/s for 7 days). Correction of the main organs of life support with respiratory support. Mixed parenteral-enteral nutrition (with the pharmacological nutrient glutamine).

Dynamics of the state: The child was on mechanical ventilation for 17 days. For 2 weeks, purulent effusion from the left pleural cavity and pericardium is daily 45–50.0 ml and 10 ml, respectively. Flushing of the pericardium and left pleural cavity with antibiotics was carried out for 2 weeks. Functioning of the cutaneous-mediastinal fistula. Constant subfebrile condition. Pericardial and pleural effusion – *St. aureus*

By the beginning of 3 weeks, the child's condition began to stabilize, according to the general condition and according to the results of the dynamic examination, there was a clear positive trend. Decrease in signs of organo-systemic damage. Clinical and biochemical analyzes: Hb 117 g/l; Blood leukocytes – $9.8 \times 10^9/l$, ESR – 13 mm/h. Total protein – 58.8 g/l; Urea – 7.2 mmol/l; AST – 1.0; Procalcitonin – 1.7 ng/ml. After 4 weeks, the child was transferred to a specialized surgical department, where an operation was performed on adhesions (decortication of the lungs).

4. Discussion of research results

According to international protocols [23–31], confirmed sepsis / SS requires rapid provision of venous access and initiation of infusion (vasopressors, if necessary), administration of antibiotics 1-3 hours before sampling for microbiological examination. Studies have shown a correlation between increased mortality and delayed ABT prescription after sepsis / SS is identified. In children, a 1 hour delay in antibiotic treatment is independently associated with increased mortality [9, 33].

In our work, against the background of antibacterial therapy, according to the data of local microbiological monitoring, by the 4th day of illness, a decrease in blood leukocytes by 19 %, procalcitonin and CR protein by 19.3 % and 21 %, respectively, was revealed. By the 8th day of intensive therapy, there was a significant stabilization of many of the studied homeostasis indicators. Procalcitonin and CR-protein at the 3rd stage of the study decreased by 30.8 and 55.9 % in relation to the initial data of the 1st stage. The results of the pSOFA assessment in septic patients showed a tendency towards a decrease in signs of organo-systemic damage from stage 1 to stage 3: 9 points – 7 points – 4 points, respectively. Procalcitonin correlated with the severity of the patient's condition on the pSOFA scale.

In addition, the inclusion of glutamine in nutritional support for patients with surgical sepsis contributed to a decrease in intoxication, a decrease in hypercatabolism and the restoration of nutritional status at the study stages, which confirms the studies of other authors on the need to include glutamine in the parenteral-enteral nutrition program to prevent mucosal atrophy, stimulate the immune function of the intestinal lymphoid apparatus and the reduction of bacterial translocation [34].

An integral part of our treatment was early immunocorrective therapy with intravenous immunoglobulins G. In sepsis, the state of immunosuppression leads to the development of secondary immunodeficiency and worsens the

prognosis, therefore today IVIG is positioned as second-line drugs in demand in patients with an unfavourable course of the disease, resistance of pathogens to antimicrobial drugs and a high-risk death [35]. In patients on the background of intensive therapy with IVIG (Bioven), an increase in immunoglobulins G was observed by the 4th and 8th days of intensive therapy by 9.5 % and 16.5 %, respectively.

Stabilization of the patient's condition was noted in 86 % of cases. The transfer of patients from the ICU was decided individually based on a comprehensive assessment of the dynamics of the patient's condition. The main criteria for the transfer of the patient to the surgical department were: positive dynamics of the course of the pyoinflammatory process (sanitation of the focus of infection), no signs of a systemic inflammatory reaction, decreased leukocytosis, procalcitonin value ≤ 0.5 ng / mg, and the sum of pSOFA points ≤ 3 . The study of procalcitonin at the stages of the study showed that with timely sanitation of the pyoinflammatory focus and adequate etiologic antibiotic therapy, this biomarker tends to decrease.

5. Conclusions

Thus, both gram-positive and gram-negative microorganisms are involved in the development of surgical sepsis in children, and the proportion of the latter is increasing. The most common pathogens of blood cultures were *Staphylococcus*, coagulase-negative and *Staphylococcus aureus* (68.4 %); in other studied loci *Ps.aeruginosa*, *Kl. pneumoniae* and *Acinetobacter* (surgical drains, peritoneal fluid 76 %, bronchoalveolar aspirate 64 %). Given the high proportion of multi-resistant flora, empirical combined deescalation of ABT with broad-spectrum antibiotics was prescribed, followed by its revision based on microbiological monitoring and clinical and laboratory data of a patient with sepsis. Despite the fact that the developed protocol for intensive therapy of sepsis adheres to the basic principles of ABT (immediate initiation after detection of sepsis, empirical antibiotic therapy, its correction after a positive bacteriological analysis, the use of the evidence base in the treatment of gram-positive and gram-negative bacteria), the mortality rate in surgical sepsis was 13 % (10 patients with widespread peritonitis, severe concomitant traumatic brain injury, cerebral coma with irreversible neurological disorders; urosepsis, chronic renal failure after repeated surgical interventions due to the development of refractory shock against the background of gram-negative surgical sepsis).

In 86.3 % of cases, the effectiveness of complex intensive therapy for surgical sepsis was noted. Early diagnosis of sepsis, rational early antibiotic therapy under the control of microbiological monitoring, non-aggressive infusion therapy with early prescription of vasopressors (SS) with constant monitoring of the main organs of the child's life support – contribute to an improvement in sepsis outcomes and a decrease in mortality.

Conflict of interests

The authors declare that they have no conflicts of interest.

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