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Research Article

Impedancemetry in the Anaesthetic Risk Assessment in Children with Acute Lymphoblastic Leukemia

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Abstract

Summary: Impedancemetry in the anaesthetic risk assessment in children with acute lymphoblastic leukosis.

Objective: to evaluate the appropriateness of using bioimpedancemetry in the complex of anesthesiological examination of children with ALL

Annotation: The article describes the issues of improving the methodology for assessing the severity of the condition and anesthetic risk of patients with acute lymphoblastic leukemia. Bioimpedancemetry reveals significant tissue imbalance, nutritional disorders, risks of dehydration and hypovolemia. A decrease in the functional reserves of the cardiovascular system was revealed against the background of chemoradiation therapy.

Conclusion: Based on the study, the author suggests the use of bioimpedancemetry in the complex of preoperative examination in patients receiving chemoradiotherapy.

Keywords: *Body Composition Analysis; Bioimpedancemetry; Acute Lymphoblastic Leukemia; Echocardiography; Anesthetic Risk; Children*

Introduction

Acute lymphoblastic leukemia takes a leading place in the oncological diseases structure in children, accounting for about 25% of the total number of malignant tumors of childhood. The five-year unobstructed survival rate of these patients currently reaches 80% as a result of treatment protocols improving [1,2].

At the same time, the prolonged use of chemo- and radiation therapy is characterized by high aggressive potential in conditions of an active oncological process [3]. According to the data published by M. S. Zinter (2014), about 40% of children with cancer need of at least one hospitalization in the intensive care unit in the first three years after diagnosis.

The mortality rate during the development of critical conditions in children with cancer is 13 - 27% and significantly exceeds the average population values [1]. The provision of the necessary volume of medical care supposes anesthetic support of a complex of diagnostic and therapeutic procedures carried out in conditions of reduced functional reserves, primarily of the cardiovascular and respiratory systems [4-7].

The mechanism of cardiovascular failure development as a dose-dependent effect in response to the use of anti-cancer medications has not been fully established [4]. There is evidence in the specialized literature that apoptosis of cardiomyocytes plays an important role in the pathogenesis of complications. The selectivity of myocardial damage is due to the limited reserves of its intracellular antioxidant protection compared to other organs and tissues. Talking about cardiomyopathy there are three clinical options, the risk of which should be taken into account in anaesthetic practice: acute heart muscle damage (24 - 48 hours after the application of cytostatic drugs), subacute damage to the heart muscle (6 - 8 months after completion of therapy with a peak of clinical manifestation after 3 - 4 months after the last dose of cytostatic drugs), delayed damage to the heart muscle (5 years or more after the last dose of cytostatics). [5].

A prerequisite for the safe use of drugs for general anesthesia is to predict the risk of hypovolemia. Particular emphasis should be placed on the fact that gastrointestinal complications account for up to 80% of all side effects of chemotherapy. Nausea, vomiting, diarrhea, mucositis are characterized by a water-electrolyte balance disorder, impaired absorption in the gastrointestinal tract, as well as a limitation of fluid and food intake due to pain in the oral cavity [8,9].

Lungs vulnerability is due to the high level of metabolism in the lung tissue, during which the active formation and release of free radicals occurs. Currently, the list of drugs that can cause drug-induced lung damage is extremely wide and includes more than 300 drugs [6]. The risk factor for obvious complications is the use of high doses of cytostatic drugs, repeated courses of chemotherapy, radiation and oxygen therapy [7]. Neurotoxicity is one of the specific systemic complications of chemotherapy, affecting both the quality of life of cancer patients and the very possibility of conducting a vital antitumor treatment. The manifestations of neurotoxicity during chemotherapy are diverse in severity and localization - from mild paraesthesias to severe lesions of the peripheral nervous system (distal sensory, motor, sensorimotor polyneuropathy), autonomic nervous system and central nervous system (encephalopathy, etc.) [5]. Obviously, monitoring of systemic disorders severity in children with cancer is one of the areas of anesthetic management of the diagnostic process, the practical implementation of which is largely achieved through the use of non-invasive methods.

In our opinion, the inclusion of a bio-impedance analysis based on measuring the bioelectric resistance of body tissues in combination with other methods of examination a child in the plan of an anaesthetic examination allows increasing objectivity in assessing the child's volemic status, as well as the functional reserves of the cardiovascular system. The expanded scope of research is due to the imperfection of existing scales and point systems for assessing the patient's condition in pediatric anesthesiology-resuscitation [10].

Purpose of the Study

The purpose of this study was to justify the appropriateness of using bioimpedancemetry in the complex of anesthesiological examination of children with ALL.

Materials and Methods

We examined 27 patients diagnosed with ALL at the stages of special treatment aged 5 to 17 years (median 10 years), 19 boys (70.4%) and 8 girls (29.6%). The patients were in the clinical departments (not ICU) and the short-term stay department (outpatient clinic). Each patient was examined twice - median 73 days. Nine children (33%) received chemotherapy using the ALL - MB 2008 protocol.

Hematopoietic stem cell transplantation (HSCT) was performed in 18 patients (67%). To 5 (27.7%) of these performed allogeneic HSCT from an HLA-compatible related donor, 9 (50%) HSCT from an HLA-compatible unrelated donor, 2 (11.1%) allogeneic HSCT from a haploidentic donor, 2 (11.1%) - HSCT from a not fully compatible unrelated donor. In 5 children (28%), the first measurement took place before HSCT (from 2 to 114 days, median 9 days). In the remaining 13 (72%), the first measurement took place after HSCT, from 1 to 411 days, the median was 56 days. The interval between HSCT and the second measurement ranged from 19 to 447 days, median 137 days.

To assess quantitative changes in the tissue composition of the body, the bioimpedancemetry method is widely used to monitor nutritional disorders and allows to assess the state of the body's water sectors. [11]. Bioimpedance analysis (BIA) was carried out using an ABC-01 instrument (Medass, Moscow). The measurements were carried out according to the standard scheme at a probe current frequency of 50 kHz, in the supine position with the application of adhesive disposable measuring electrodes in the area of the right wrist and ankle joints. According to the implemented in the instrument software formulas, a number of indicators are automatically calculated that characterize the body's tissue composition: body fat mass (BFM), "Lean" body mass (LM), skeletal muscle mass (SMM), and the amount of active cell mass (ACM) and phase angle (PhA). ACM is a collection of body cells that consume the bulk of oxygen, emit a large part of carbon dioxide, that is, are actively involved in the metabolism of proteins, fats and carbohydrates, PhA (the arctangent of the ratio of reactive and active resistance of body tissues, measured at a frequency of 50 Hz.) characterizes the state cell membranes.

For a unified calculation and correct comparison of indicators in different patients, based on the obtained values of bio-impedance indicators, the body fat mass index (BFMI) was calculated by the formula: BFMI = FM (kg)/height^2 (m^2); skeletal muscle mass index (SMMI) according to the formula: SMMI = SMM (kg) / height^2 (m^2); active cell mass index (ACMI) according to the formula: ACMI = ACM (kg)/ height (m).

The indication for repeated bioimpedancemetry was a moderate negative dynamics of echometric indicators (subclinical changes), revealed by dynamic observation.

A significant effect on the volemic status (the formation of edema) can be caused by circulatory failure, which is formed in patients with cancer during chemoradiotherapy [4,5,12], therefore, echocardiography was performed for all children to evaluate cardiac activity. It was performed using the Philips iU22 and Toshiba Aplio 500 devices using the M- and B-modes. Echometric indicators were evaluated using the Z-score calculator program recommended for use by the American Cardiography Association. [13]. Anthropometry (somatometry) was used in all patients examination. Body mass (BM) was measured on a medical balance with an accuracy of 100 g, body length was determined with a height meter with an accuracy of 0.5 cm. BMI body mass index was calculated by the formula: BMI = BM (kg)/height^2 (m^2).

An exact one-sided sign criterion was used for statistical processing. The Spearman rank coefficient was used to assess the correlation of parameters.

Results and Discussion

Growth has not changed during the observation period (Table 1). However, it was revealed a decrease in body weight of children. Body weight in the first measurement ranged from 19.3 to 85.3 kg (median 38.2 kg) and from 18.7 to 87.6 kg (median 33.0 kg) in the second. BMI in the first dimension was determined to be in the range from 13.00 to 26.00 (median 16.70) and from 12.00 to 26.00 (median 15.60) in the second dimension. The differences are significant ($p < 0.05$).

The substrate of active resistance in a biological object are liquids (both extra- and intracellular) with an ionic conduction mechanism. By the value of active resistance, the total body water percentage (BW) is calculated, the high conductivity of which is due to the presence of electrolytes in it. In our studies, the resistance index (R50) in the first dimension ranged from 575.30 to 1229.00 Ohms (median 812.30 Ohms) and from 616.50 to 1239.00 Ohms (median 855.60 Ohms) in the second dimension. The reactance index (Xc50) in the first dimension ranged from 25.10 to 81.50 Ohms (median 48.80 Ohms) and from 29.50 to 66.10 Ohms (median 47.30 Ohms) in the second dimension. The results fixed indirectly indicate the absence of significant changes in the rate of metabolic processes, as well as the permeability of cell membranes. In the complex assessment of other general clinical indicators (the severity of intoxication syndrome, the peculiarities of the temperature reaction in a child, sweating, etc.), we considered these characteristics as one of the indicators of the absence of significant complications of the pathological process. It should be noted that the magnitude of the reactive component of the impedance is calculated values of the basic metabolism (BM) and ACM.

The software of the ABC-01 device (Medass, Moscow) allows us to calculate the quantitative change in tissue in% of normal. Changes in the FM parameter in% of the norm in the first dimension were from 59.90 to 311.70% (median 122.00%) and from 41.00 to 312.00% (median 125.40 in%) in the second. The violation of fat metabolism, expressed in the absolute and relative increase in fat mass, in our opinion, is associated with the use of glucocorticosteroids in the treatment of children with ALL.

Body LM in the first measurement ranged from 13.40 to 58.30 kg (median 26.60 kg) and from 13.70 to 56.70 kg (median 22.30 kg) in the second measurement. Changes in the LM parameter in% of normal ranged from 58.80 to 100.60% (median 80.50%) in the first dimension and from 57.40 to 99.90% (median 73.50%) in the second. Thus, in all measurements, a decrease in the listed indicators relative to reference values was revealed.

Taking into account the direct relation to the basic metabolism, constitution, and physique of a person, LM is characterized by a high specific metabolic activity, as well as a relatively constant value of hydration. A decrease in the level of LM in patients with cancer can be an anorexia-cachexia syndrome's manifestation [14]. Of course, we did not record such significant clinical manifestations, however, dynamic observation revealed a tendency to reduced nutrition, apparently due to a decrease in appetite in cancer patients and impaired function of the gastrointestinal tract during chemoradiotherapy.

Indicators	First measurement	Second measurement
Height (m)	1,43 (1,06 - 1,48)	1,43 (1,06 - 1,48)
Weight (kg)	38,20 (19,30 - 85,30)	33,00 (18,70 - 87,60)
BMI (kg/m^2)	16,70 (13,00 - 26,00)	15,60 (12,00 - 26,00) *

Table 1: *Anthropometry significant differences (p < 0,05).*

Indicators	First measurement	Second measurement
BFM (kg)	10,00 (3,80 - 30,50)	9,10 (2,80 - 30,907)
LM (kg)	26,60 (13,40 - 58,30)	22,30 (13,70 - 56,70)
ACM (kg)	7,80 (3,30 - 28,10)	7,20 (3,00 - 25,50)
PhA (degrees.)	3,20 (1,70 - 5,40)	3,00 (1,70 - 4,70)

Table 2: *Bioimpedansometry.*

We found a decrease relative to the reference values of all indicators characterizing the SMM (first and second measurements, respectively): body SMM from 3.90 to 30.70 kg (median 13.20 kg) and from 4.10 to 29.30 kg (median 12, 20 kg), SMMI - from 3.47 to 9.0 (median 6.37) and from 3.65 to 7.85 (median 5.82), SMM% of norm - from 59.00 to 104.10% (median 80.50%) and from 54.70 to 94.40% (median 75.80%). Similar trends were established in the analysis of bioimpedance parameters reflecting the state of ACM (first and second measurements, respectively): body ACM - from 3.30 to 28.10 kg (median 7.80 kg) and from 3.00 to 25.50 kg (median 7.20 kg), ACMI - from 2.40 to 12.80 (median 6.37) and from 2.17 to 10.57 (median 4.82), AKM% of norm - from 16.20 to 83, 20% (median 51.00%) and from 17.20 to 75.00% (median 43.20%) in the second. A decrease relative to the reference values was revealed. In the analysis of the results obtained, more attention should be paid to the fact that ACM is well hydrated because it contains metabolically active tissue. Anatomically, these are smooth and skeletal muscles, myocardium, gastrointestinal tract, blood cells, nervous system, kidneys, and skin. Active cell mass may decrease with protein deficiency, correlates with the body potassium level. It is important that the clinical significance of ACM is associated with the possibility of indirectly assessing the state of metabolism [15,16].

PhA of impedance is used to assess the functional state of the body, the intensity of metabolic processes and violations of nutritional status. According to the literature [17], the phase angle is an independent criterion for malnutrition, functional status and prognostic survival criteria in cancer patients. A decrease in the indicator below 5 is associated with a decrease in muscle strength, a deterioration in the quality of life and an increase in mortality in patients with advanced cancer [18] and in patients with chronic kidney diseases [19]. Our studies showed a significant decrease in the phase angle: in the first measurement, it varied in the range from 1.70 to 5.40 (median 3.20 deg.), In the second - from 1.70 to 4.70 (median 3.00 deg.). The latter allowed us to formulate the conclusion that the decrease in nutrition that we detected led to a clinically significant deterioration in nutritional status in all examined children, which is also confirmed by a significant decrease in BMI (Table 1).

Bioimpedansometry characterizes the water sectors of the body [20]. During dynamic observation, we did not establish any significant differences in the initial and repeated measurements of indicators (BW, kg): from 10.20 to 42.70 kg (median of 19.20 kg) and from 10.20 to 41.50 kg (median of 16.30 kg), extracellular fluid (ECF, kg): from 5.90 to 17.90 kg (median 9.40 kg) and from 5.90 to 17.60 kg (median 8.40 kg), intracellular fluid (ICF) from 4.30 to 24.80 kg (median of 9.80 kg) and from 4.30 to 23.90 kg (median of 8.00 kg). There was no significant difference in the initial and repeated measurements and the centile distribution indicators: BW percentile - from 0.50 to 91.50 perc (median 22 perc) and from 0.50 to 90.50 perc (median 19 perc), ECF perc - from 1 to 96 perc (median 37 perc) and from 1 to 95 perc (median 24 perc), ICF perc - from 1.00 to 94 perc (median 22 perc) and from 1 to 92 perc (median 21 perc).

The data presented indicate a high and time-stable risk of dehydration, which has an obvious connection with a decrease in the body's content of well-hydrated tissue (LM, ACM). This fact explanation, most likely, is associated with a change in the structure of adipose tissue (edema), which is possible with hypoalbuminemia, obesity and cardiovascular diseases [21,22]. Changes in the body's total water parameter in% of the norm (BW% of the norm) in the first dimension were from 139.60 to 517.80% (median of 207.40%) and from 143.60 to 524.20% (median of 197.50%) in the second dimension (Table 3).

Indicators	First measurement	Second measurement
Z-score	-0,41 (-5,40 - 0,98)	-0,69 (-2,23 - 2,09)*
EF (%)	70,00 (57,00 - 82,00)	67,00 (60,00 - 77,00)*
RA D (mm)	25,40 (10,00 - 32,00)	26,00 (20,00 - 31,00)
RV D (mm)	23,85 (16,00 - 29,60)	23,00 (18,50 - 29,50)
RA D (mm)	24,20 (2,47 - 33,70)	25,70 (20,00 - 34,30)*

Table 3: *Echocardiography iindicators.*

Echocardiography was evaluated using the Z-score calculator program recommended for use by the American and European cardiography associations [23].

Indicators of body surface area (BSA, m^2) at the stages of treatment remained virtually unchanged. In the first dimension, the variation was from 0.75 to 1.77 m^2 (median 1.15m^2) and from 0.75 to 1.76m^2 (median 1.15 m^2) in the second. At the stages of the examination, the final systolic size of the left ventricle (FSS, mm) varied from 18.5 to 34.9 mm (median 23.6 mm) and from 18.5 to 31.5 mm (median 25.9 mm), the final diastolic size (FDS, mm) from 28.0 to 49.9 mm (median 38.9 mm) and from 32.4 to 52.0 mm (median 39.5 mm). We have established significant changes in the Z-score of the left ventricle ($p < 0.05$): in the first measurement, it was determined in the range from -5.40 to 0.98 (median -0.41), with a second - from -2,23 to 2.09 (median -0.69), as well as ejection fractions (EF%) in the initial measurement from 57.00 to 82.00% (median 70.00%), in the second - from 60.00 to 77.00% (median 67.00%). The diameter of the left atrium (D mm) in the first dimension varied from 10.00 to 32.00 mm (median 25.40 mm) and from 20.00 to 31.00 mm (median 26.00 mm) in the second. The Z-score of the left atrium in the first dimension was found to be in the range from -7.00 to 1.57 (median -0.09) and from -1.86 to 1.24 (median -0.27) in the second. Changes in the diameter of the right ventricle (D mm) in the first dimension ranged from 16.00 to 29.60 mm (median 23.85 mm) and from 18.50 to 29.50 mm (median 23.00 mm) in the second. The diameter of the right atrium (D mm) in the first dimension varied from 2.47 to 33.70 mm (median 24.20 mm) and from 20.00 to 34.30 mm (median 25.70 mm) in the second. The differences are significant ($p < 0.05$).

As follows from the presented data, the echometric parameters remained within the reference values, although their changes against the background of special treatment were in the nature of negative dynamics. To identify the correlation of echometric data and BIA indicators, the Spearman rank coefficient was used. It should be noted that we have revealed a moderately close relationship ($r = 0.41$) between the EF index and the calculated BIA - FR% normal in the first dimension.

Conclusion

1. The BMI decreasing during special treatment is due to a significant tissue imbalance, manifested in a moderate decrease in lean mass, musculoskeletal muscle mass, a significant decrease in active cell mass and an increase in (absolute and relative) adipose tissue content.
2. There is an increased risk of developing dehydration and hypovolemia in children with chemoradiotherapy, which may be associated with impaired water-electrolyte metabolism, as well as with a decrease in the content of well-hydrated tissues in the body, such as muscle.
3. Due to special treatment, a tendency has been established to reduce the reserves of the cardiovascular system, which is reliably confirmed by a decrease in the ejection fraction and an increase in the diameter of the right atrium; a decrease in the ejection fraction may indirectly indicate the development of hypovolemia in children with chemoradiotherapy.
4. The data obtained allow us to justify the appropriateness of using bioimpedancemetry in the complex of anaesthetic examination of children with ALL in order to predict the risks of complications and develop approaches to their prevention and correction.

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