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Automation of Intraoperative Analysis of the Indicators of the Inflammatory Response of Neurosurgical Patients Undergoing Brain Tumor Removal:

Information Processing, Analysis, Prognosis

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ABSTRACT

The data of the study of indicators of the inflammatory response, hormonal status, biochemical blood parameters in the perioperative period in neurosurgical patients undergoing surgery for tumors of the posterior cranial fossa are presented. The study included 65 patients. The operations were performed under anaesthesia using fentanyl (3-5 μg/kg-hour), clonidine (1-2 μg/kg-hour), and propofol (3-5 mg/kg-hour). A significant increase in the level of Interleukin 10 was noted at the stage of hemostasis. The next day after the operation, the level of Interleukin 6 was significantly increased. At the stage of hemostasis, a transient increase in the levels of ACTH, Cortisol, Prolactin was noted. Their rates returned to the initial levels on the next day after the operation. Under conditions of neurovegetative stabilization, a sufficient humoral response to surgical trauma was noted.

KEYWORDS

Inflammatory Response, Information, Modeling, Neurovegetative, Operations, Posterior Cranial Fossa, Stabilization, Systemic

INTRODUCTION

Describe the general perspective of the article. End by specifically stating the objectives of the article.

The digitalization of the medical sector in the Russian Federation is currently of a systemic nature, mainly at the level of federal documents, not being comprehensive, often focusing on specific local areas. At the same time, part of the processes that are not included in the priority list require phased automation in order to ensure timeliness and control the completeness of operations with information, as well as to optimize time costs and minimize the human factor. An example of such an area is the

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intraoperative control of neurosurgical patients. In the Almazov National Medical Research Center, the area of research for the designated subject area is the control of the inflammatory response in the perioperative period when brain tumors are removed.

Significant research and practical testing of the developed approaches for working with patients allowed creating a sufficient data sample, on the basis of which, following the basic principles of building distributed information systems, with the prospect of developing to the big data level, specialists of information departments of Admiral Makarov State University of Maritime and Inland Shipping developed the information system called "Automated system of intraoperative monitoring of homeostasis index of neurosurgical patients" (Sokolov, Lesteva & Musin, 2014).

Information technology is now widely used. It is clear that such an important area of human life as health care cannot be left out. The latest digital developments have a positive effect on the development of the most promising methods of organizing the provision of medical care to the population around the world. At the same time, the effective construction of IT infrastructure is becoming increasingly important. Many states have long been active in innovating in the medical field.

SUBJECT OF THE STUDY

There is a certain set of body reactions in which the functional state called the "surgical stage of anesthesia" is reflected and to which the anesthesiologist most often draws attention and tries to correct. These are indicators of systemic hemodynamics, changes in spontaneous and induced bioelectric activity of the brain, deviations in the level of various hormones and other biologically active substances in the blood.

In neurosurgery, the concept of the adequacy of anesthesia is interpreted more broadly. So, the criteria of adequacy in neuroanesthesiology, depending on the stage of the operation, can be: before decompression of the brain - maintaining perfusion pressure; after decompression - preservation of elasticity, suppleness of the brain, assessment and the maximum possible limitation of centrogenic reactions; at the stage of removal of the tumor and hemostasis - normal indicators of vascular-platelet and coagulation hemostasis in the wound. In addition, an adequate anesthetic benefit is the key to a smooth, harmonious exit of the patient from the anesthetized state. In the postoperative period after surgery on the brain, the clinical manifestations of inadequacy of anesthesia can be: excessive inhibition of central nervous system functions, multiple organ dysfunction. Apparently, an overly expressed systemic inflammatory response may be the background, and in some cases, the main cause of this symptomatology. For cognitive impairment, this relationship is well established (Sokolov, Lesteva & Musin, 2014).

Inflammation is both a pathological and adaptive process caused by the reaction of the body's defense mechanisms to local damage. Inflammation triggers - tissue degradation products, immune complexes - activate several basic components of the inflammation program at once. Moreover, the initial activation of even one link can "turn on" the entire system of inflammatory reactivity as a whole. The regulatory intermediaries for this mutual activation are cytokines, hemostatic activation products, biogenic amines, and many other inflammatory mediators. A key role in coordinating the mechanisms of inflammation belongs to cytokines. The main producers of cytokines are T cells and activated macrophages, as well as other types of leukocytes, postcapillary venule endotheliocytes, platelets and various types of stromal cells. Initially, a local inflammatory response is controlled by proinflammatory cytokines such as IL-1, IL-6, IL-8, IL-12, TNF, interferons, as well as their endogenous antagonists, especially IL-10. Subsequently, with the prevalence of the inflammatory component over the anti-inflammatory one and damage to the primary barrier structures in the area of inflammation, a "breakthrough" of inflammatory mediators into the systemic circulation occurs. At the same time, the main function of pro-inflammatory mediators in the circulating blood is to attract white blood cells, coagulation and complement factors, acute phase proteins to the area of inflammation in order to perform a protective and then recovery function of the inflammatory process (Konsman, Luheshi, Bluthe, & Dantzer, 2000).

Non-infectious reasons for the manifestation of a systemic inflammatory response can include: ischemia, reperfusion (after hemorrhagic shock), the use of VAD in cardiac surgery, severe pancreatitis, intestinal ischemia (mesenteric vascular thrombosis), but the most common causes are severe trauma or extensive surgery (Savel'ev & Gel'fand, 2013).

There are neuro-reflex (realized by the sympathetic nervous system) and humoral ways of informing the central nervous system about inflammation. The humoral chain is as follows. The antigen initiates the synthesis of pro-inflammatory cytokines by peripheral macrophages, then the synthesis of pro-inflammatory cytokines in the choroid plexuses of the ventricles begins. A cytokine-mediated effect on the neuroregulatory centers of the brain occurs both through the microglia of afferent pathways of cranial nerves (mainly n.vagus) and through the cerebrospinal fluid. The efferent effects of this cascade of reactions are realized through the neuroendocrine response, fever, various disorders of behavior, consciousness, etc. Thus, the adaptive effect of the systemic inflammatory response to surgical damage is realized (Konsman, Luheshi, Bluthe, & Dantzer, 2000).

Adaptive reactions are a chain of neuro-humoral changes that lead to the mobilization of the hypothalamic-pituitary system and the release of catecholamines, ACTH, ADH, and TSH into the blood. The purpose of these reactions is to quickly protect the body from pathological effects.

Most neuroregulatory systems that play a role in adapting the body to various environmental influences are located in the brain stem. Opioid and adrenergic antinociceptive systems are integral parts of the neuroregulatory systems of the brain stem. They contribute to the functional integration of numerous compensation and adaptation mechanisms. The introduction of opioids in combination with clonidine forms a sufficient level of neurovegetative stability due to the modulating effect of drugs on the neuroregulatory structures of the brain stem (Savel'ev & Gel'fand, 2013). Under the conditions of an anaesthetic support based on the use of such a combination of drugs, an adequate intraoperative assessment of both hemodynamic reactions and electrophysiological parameters and determination of the indications for continued neurovegetative stabilization in the postoperative period based on this assessment are possible.

The aim of the research was to study biochemical, coagulation indicators, systemic inflammatory response data (including cytokine levels), hormonal status in patients who had surgery for tumors of the posterior cranial fossa under conditions of neuro-vegetative stabilization based on the combined administration of fentanyl and clonidine.

MATERIALS AND METHODS

The study sample included 65 patients (42 women, 23 men). The average age of the studied patients was 50.5 ± 5.2 years. All patients had surgery for tumors of the posterior cranial fossa. The operations were performed as planned. The following histological variants of tumors of the posterior cranial fossa were distinguished: meningiomas, neuromas of the VIII nerve, ependymomas, astrocytomas. The preoperative condition of all patients was assessed as severe due to the underlying disorder, compensated for by vital functions and corresponding to classes III - IV of the physical condition of patients according to the classification of the American Society of Anesthesiologists (ASA). Patients without severe somatic pathology were selected into the study group. All patients were treated in the neuro-oncology department of the Russian Research Neurosurgical Institute named after prof. A.L. Polenov in the period from 2011 to 2014.

The operations were performed under conditions of neuro-vegetative stabilization using an opioid analgesic and alpha-2-adrenoagnosis. To induce anesthesia, fentanyl (3.5-7.0 μg/kg), clonidine (1.4-2.8 μg/kg) and propofol (2-3 mg/kg) were administered (Arumugam, Shiels, Woodruff, Granger & Taylor, 2004). To maintain anesthesia, fentanyl (3-5 μg/kg-hour), clonidine (1-2 μg/kg-hour) and propofol (3-5 mg/kg-hour) were infused. Pipecuronium bromide was used as a muscle relaxant. The operations were carried out under mechanical ventilation in the standard ventilation mode.

Laboratory studies included: analysis of blood biochemical parameters, coagulogram data, hormonal status indicators (TSH, T3, T4, ACTH, Cortisol, STH, Prolactin), cytokine levels (IL-8, IL-6, IL-10, TNF). Studies of blood biochemical parameters and hormone levels were carried out using an Integra 400 plus biochemical analyzer (Roche, Switzerland, Germany, USA). Studies of cytokine levels were carried out using an Immuite 1000 immunochemiluminescent analyzer (DPC, USA). Analysis of blood samples was carried out in five stages: a day before surgery, on the day of surgery before induction of anesthesia, after induction of anesthesia, after removal of the tumor (at the stage of hemostasis), on the first day after surgery. These stages were chosen in order to assess the influence of various factors of the perioperative period on the neurohumoral indicators of adaptive reactions of the body.

AUTOMATION OF THE STUDY. BASIC INFORMATION

The developed automated system allows processing the results of the study. The system has the following scheme (Figure 1).

The reference system for accounting indicators includes 3 main subsystems, 2 of which also include a certain number of modules. The main subsystems: “Data viewing”; “Add new data”; “Data analysis”. The data viewing subsystem includes the following modules: “Search for necessary data”; “Change of data”; “Data removal”. The data analysis subsystem has 2 modules: “Comparison of indicators” and “Plotting”.

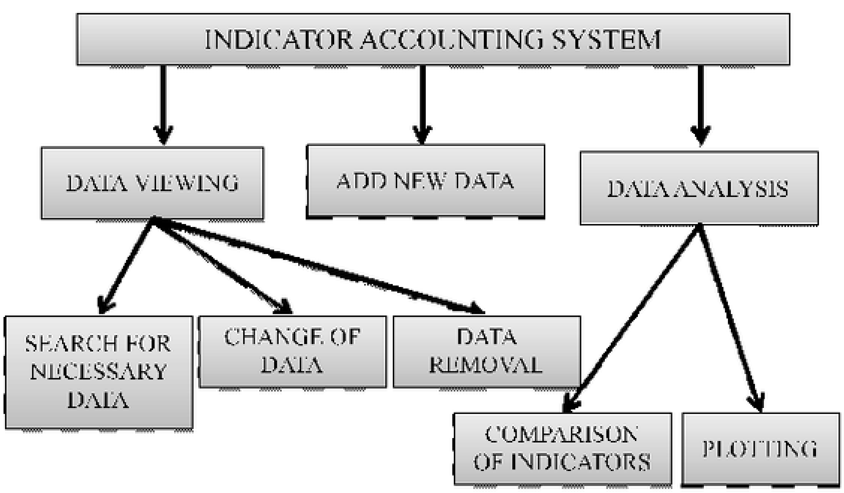
The interface of the developed automated system reflects all the necessary subsystems and modules of the developed reference system.

For information processing, a table with general data is used. MS Excel is used to work with it. Due to that it was possible to plot graphs using one of various types of interpolation and approximation in order to obtain forecasts.

To build the forecast curves, approximation and interpolation methods are used.

Interpolation - in computational mathematics, a way of finding intermediate values of a quantity from an available discrete set of known values.

Figure 1. The structure of the indicator accounting system



Linear interpolation — interpolation by the algebraic binomial $P1(x) = ax + b$ of the function f given at two points x_0 and x_1 of the segment [a, b]. If values are specified at several points, the function is replaced by a piecewise linear function.

Geometrically, this means replacing the graph of a function f with a line passing through the points $(x_0, f(x_0))$ and $(x_1, f(x_1))$.

The equation of such a straight line has the form:

$$\frac{y - f\left(x_0\right)}{f\left(x_1\right) - f\left(x_0\right)} = \frac{x - x_0}{x_1 - x_0}.$$

from here for $X \epsilon\ [x_0, x_1]$ it follows that

$$F(x) \approx y = P_1(x) = f(x) + \frac{f\left(x_1\right) - f\left(x_0\right)}{x_1 - x_0}(x - x_0).$$

This is the linear interpolation formula, while

$$F(x) = P_1(x) + R_1(x)'$$

where $R_1(x)'$ — formula error:

$$R_1(x) = \frac{f''\left(\psi\right)}{2}\left(x - x_0\right)\left(x - x_1\right), \psi\epsilon\ [x_0, x_1].$$

The following estimate is fair

$$|R_1(x)| \leq \frac{M_2}{2}\max\left|\left(x - x_0\right)\left(x - x_1\right)\right| = \frac{M_2h^2}{8},\ \ M_2 = \max_{[a,b]}\left|f'\,'\left(x\right)\right|, h = x1 - x0.$$

Piecewise constant interpolation.

On each segment $[x_{2-1}, x_2]$, the interpolation polynomial is equal to a constant, namely, the left or right value of the function.

For left piecewise linear interpolation $\left(x\right) = f_{i-1},\ if\, x_{i-1,} \leq x < x_i,$ $F(x) = f_{i-1}$, if $x_{i-1} <= x < x_i$, i.e.

$$F(x) = \begin{cases} f_0, x_0 \leq x < x_1 \\ f1, x_1 \leq x < x_2 \\ \ldots\ldots\ldots\ldots\ldots\ldots\ldots \\ f_{N-1}, x_{N-1}, <= x < x_N \end{cases}.$$

For right piecewise linear interpolation $\left(x\right) = f_i, if\, x_{i-1,} \leq x < x_i$, i.e. $F(x) = \begin{cases} f_1, x_0 < x <= x_1 \\ f_2, x_1 < x <= x_2 \\ \cdots\cdots\cdots \\ f_N, x_{N-1}, < x <= x_N \end{cases}$

Interpolation conditions are met. The constructed function is discontinuous, which limits its application. For left piecewise linear interpolation, we have a graphical representation:

Piecewise linear interpolation.

On each interval [xi–1, xi], the function is linear $F_i(x) = k_i x + l_i$. The values of the coefficients are found from the fulfillment of the interpolation conditions at the ends of the segment: $F_i(x_{i-1}) = f_{i-1}$, $F_i(x_i) = f_i$. We get the system of equations: $k_i x_{i-1} + l_i = f_{i-1}$, $k_i x_i + l_i = f_i$, from where we find $k_i = \dfrac{f_i - f_{i-1}}{x_i - x_{i-1}}$, $l_i = f_i - k_i x_i$. Therefore, the function F(z) can be written as:

$$F(x) = \frac{f_i - f_{i-1}}{x_i - x_{i-1}} x + f_i - k_i x_i, \text{ if } x_{i-1} \leq x \leq x_i, \text{ i.e.}$$

$$F(x) = \begin{cases} \dfrac{f_1 - f_0}{x_1 - x_0} x + f_0 - k_0 x_0, x_0 \leq x \leq x_1 \\ \dfrac{f_2 - f_1}{x_2 - x_1} x + f_1 - k_1 x_1, x_1 \leq x \leq x_2 \\ \cdots\cdots\cdots\cdots\cdots\cdots \\ \dfrac{f_N - f_{N-1}}{x_N - x_{N-1}} x + f_{N-1} - k_{N-1} x_{N-1}, x_{N-1} \leq x \leq x_N \end{cases}$$

Or $F(x) = k_i * (x - x_i-1) + f_i-1$, k_i = (fi - fi-1) / (xi - xi-1), $x_i-1 \leq x \leq x_i$, i=1,2,...,N-1.

When using linear interpolation, the interval at which the value of x falls is determined first, and then it is substituted into the formula.

The resulting function will be continuous, but the derivative will be discontinuous at each interpolation node. The error of such interpolation will be less than in the case of piecewise constant interpolation. An illustration of piecewise linear interpolation is shown in Figure 3.

Cubic interpolation spline.

Figure 2. Graph of piecewise constant interpolation

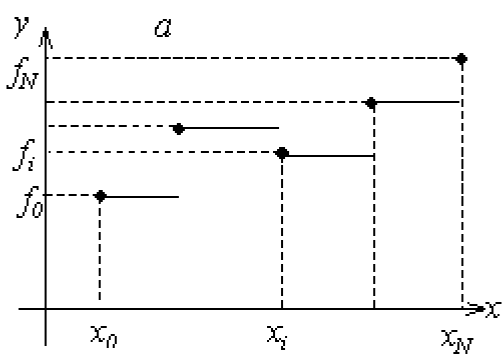
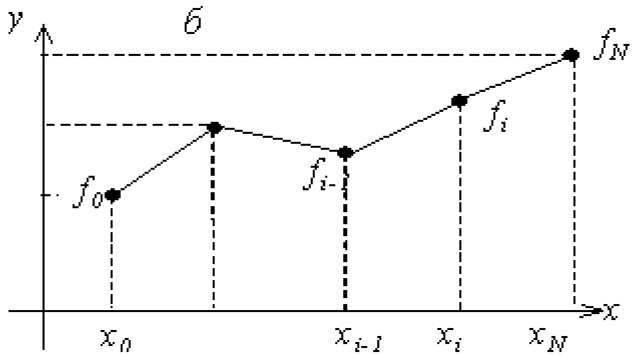


Figure 3. Graph of piecewise linear interpolation



The word spline means a flexible ruler used to draw smooth curves through given points on a plane. The shape of this universal pattern on each segment is described by a cubic parabola. Splines are widely used in engineering applications, in particular, in computer graphics. So, on every i-th segment [xi–1, xi], i = 1, 2, ..., N, we will seek a solution in the form of a polynomial of the third degree:

Si(x)=ai+bi(x–xi)+ci(x–xi)2/2+di(x–xi)3/6.

The unknown coefficients ai, bi, ci, di, i=1, 2,..., N, we will find from:

- interpolation conditions: Si(xi)=fi, i=1, 2,..., N; S1(x0)=f0,
- function continuity Si(xi–1)=Si–1(xi–1), i=2, 3,..., N,
- continuity of the first and second derivative:

S /i(xi–1)=S /i–1(xi–1), S //i(xi–1)=S //i–1(x i–1), i=2, 3,..., N.

Considering that $S_{i-1}(x) = a_{i-1} + b_{i-1}(x-x_{i-1})+c_{i-1}(x-x_{i-1})^2/2+d_{i-1}(x-x_{i-1})^3/6$, to determine 4N unknowns, we obtain a system of 4N.where hi=xi – xi–1. The missing two equations are derived from additional conditions: S //(a)=S //(b)=0. It can be shown that $c_0 = c_N = 0$. Unknown bi, di can be excluded from the system by obtaining a system of N+1 linear equations (hereinafter - SLAE) (*Kondratyev, Tsentsiper, Kondratyeva & Nazarov,* (2014).) for determining the coefficients ci:

c0 =0, cN =0,

hici–1+2(hi+hi+1)ci+h i+1ci+1=6$\left(\frac{f_{i+1}-f_i}{h_i}-\frac{f_i-f_{i-1}}{h_{i-1}}\right)$, i=1, 2,…, N–1.

In the case of a constant grid hi = h, this system of equations is simplified.

$$4c_1 + c_2 = 6\frac{f_2 - 2f_1 + f_0}{h^2};\ c_{i-1} + 4c_i + c_{i+1} = 6\frac{f_{i+1} - 2f_i + f_{i+1}}{h^2};\ i = 2,\dots,\ N-2;$$

$$c_{N-2} + 4c_{N-1} = 6\frac{f_N - 2f_{N-1} + f_{N-2}}{h^2};\ c_N = 0.$$

This SLAE has a three-diagonal matrix and is solved by the sweep method.
The coefficients b_i, d_i are determined from the formulas:

$$d_i = \frac{c_i - c_{i-1}}{h}\,;\, b_i = 1/2c_i h - 1/6 d_i h^2 + \left(f_i - f_{i-1}\right)/h\,;\, a_i = f_i\,.$$

To calculate the value of S(x) at an arbitrary point of the segment z∈[a, b], it is necessary to solve the system of equations for the coefficients ci, i = 1,2, ..., N–1, then find all the coefficients bi, di. Next, it is necessary to determine what interval [xi0, xi0–1] this point falls into, and, knowing the number i0, calculate the value of the spline and its derivatives at the point z

S /(z)=bi0+ci0(z–xi0)+di0(z–x i0)2/2, S //(z)=ci0+di0(z–x i0).

Approximation is a scientific method that consists in replacing some objects with others, in one sense or another, close to the original, but simpler (Kondratyev, 2008).

Approximation allows one to study the numerical characteristics and qualitative properties of an object, reducing the problem to the study of simpler or more convenient objects (for example, those whose characteristics are easily calculated or whose properties are already known). In the theory of numbers, Diophantine approximations are studied, in particular, the approximations of irrational numbers by rational ones. In geometry, approximations of curves by broken lines are considered. Some sections of mathematics are entirely devoted to approximations, for example, the theory of approximation of functions, numerical methods of analysis (Lesteva, 2009).

The developed software is a local program. Thus, the data processed during the program cannot get to the local network or the Internet without the knowledge of the employees working with the software. This ensures the security of data, the distribution of which entails liability, in accordance with Federal Law No. 152 of July 27, 2006 “On Personal Data”. The underlying distributed architecture can be implemented in case of compliance with information security requirements, in particular, the use of certified cryptographic tools.

AUTOMATION OF THE STUDY. PRACTICAL USE

The initial form allows going to one of three main actions, Figure 4.

On the plotting form, there are four fields to fill in with those parameters that need to be displayed on the graph. Upon activation of each of the four fields, a drop-down list of parameters opens, the indicators for which are presented in the general table.

Figure 4. Initial form

After filling in the appropriate fields and clicking the “Build chart” button, the graph is built (Figure 5).

For convenience, it is possible to close any of the provided forms using the standard button to close the window. The initial form is called up using the keyboard shortcut Ctrl + Q.

The ability to build forecasts on the schedule is carried out using standard MS Excel tools. To do this, go to the “Work with charts: Layout” tab (Figure 6).

Adding a new patient is carried out using the form for adding new data, which opens after clicking the “Add client” button on the main form (Figure 7).

The form for adding new data works with the same elements as the form for displaying information. Data is also saved using the “Save changes” button.

Comparison of client indicators.

Figure 5. Examples of built graphs

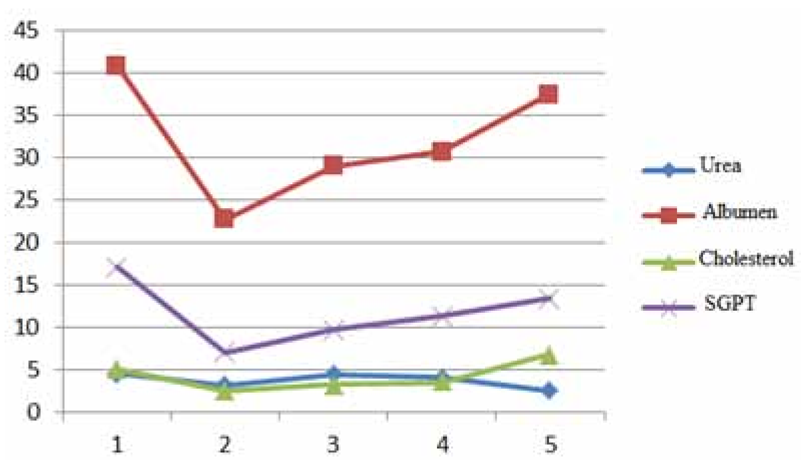


Figure 6. Graph with plotted trend lines

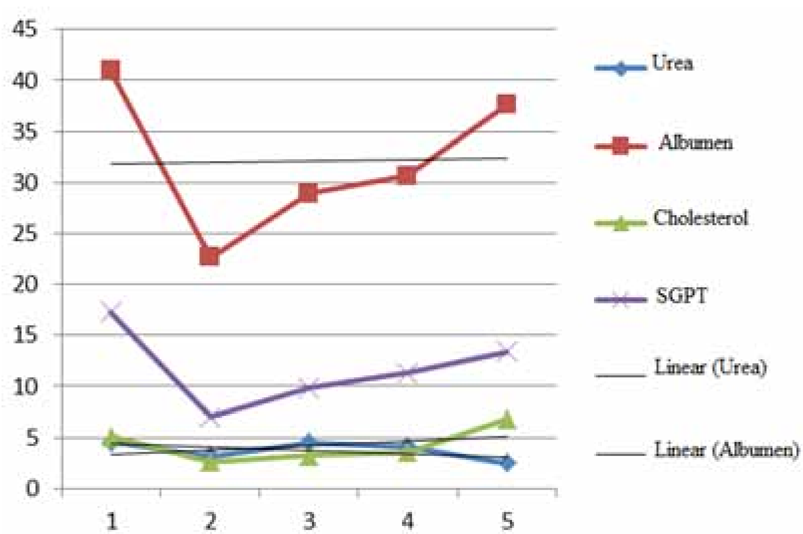


Figure 7. Form for adding new data

Clicking on the "Compare client indicators" button on the initial form will open the Client Comparison form.

There are four fields in the form for filling with the names of patients whose indicators need to be compared and a field for filling with the name of the indicator, according to which the comparison will be made (Kondratyev, Dryagina, Zhulev & Nikishchenkova, 2012).

After filling in the appropriate fields and pressing the "Compare" button, the names of the selected patients and their indicators are written out in a table where the average value of their indicators is determined, and a list is arranged in descending order of average values of indicators (Figure 8).

The automated system has the ability to set thresholds for timely notification of the user about the deviation of the current indicator from the norm.

RESULTS OF THE STUDY

In general, indicators of hormonal status, blood coagulation, and biochemical parameters remained relatively stable at all stages of the perioperative period. When studying the levels of cytokines, a significant increase in the level of Interleukin 10 at the stage of hemostasis was noted. On the next day after the operation, the level of Interleukin 6 was significantly increased.

According to the results of automated data analysis, a significant increase in creatine kinase was noted after removal of the tumor with the maximum values of this indicator on the next day after surgery. This increase was interpreted as a result of cytolysis after a surgical trauma and the entry of intracellular enzymes into the blood. An increase in the level of myoglobin in the blood after surgery, which also reached its maximum value on the first day after the operation, could be associated with an intraoperative decrease in mean arterial pressure, leading to a short-term relative hypoperfusion

Figure 8. Comparison table of indicators

	A	B	C	D	E	F	G
1	Тютькина	4,62	3,42	2,85	3,60	2,87	3,47
2	Дворников	2,67	1,99	1,64	1,74	1,48	1,90
3	Кадашников		1,90	1,34			1,62
4	Мамедов А.К.	1,10	2,33	1,56	0,85	1,57	1,48

Table 1. Dynamics of cytokine levels at various stages of the perioperative period

Indicator	Initial	Before Induction of Anesthesia	After Induction of Anesthesia	At the Stage of Hemostasis	On the First Day After Surgery
IL 8, pg/ml	12.95±1.02	10.28±0.72	9.44±0.58	10.47±0.96	9.65±0.72
IL 6, pg/ml	2.24±0.34	5.21±2.12	3.75±1.66	7.90±1.13	25.75±3.61*
IL 10, pg/ml	5.88±0.37	7.70±1.94	8.38±2.07	31.09±5.55*	9.03±1.43
TNF, pg/ml	9.07±0.53	7.90±0.41	7.74±0.43	7.84±0.43	6.49±0.38

*- p< 0.01;

during tumor removal. Similar data were obtained in previous studies conducted at the Russian Research Neurosurgical Institute named after prof. A.L. Polenov in neuro-resuscitation patients after neurosurgical operations (Sokolov, Zhilenkov, Chernyi, Nyrkov & Glebov, 2020).

In addition, at the stage of hemostasis, a transient increase in the levels of ACTH, Cortisol, Prolactin was noted, the rate of which returned to the initial values on the next day after the operation. These changes fit into the standard picture of changes in hormonal status in response to surgical trauma.

Currently, medical information systems (information systems) are developing more and more actively, which helps healthcare institutions to work more efficiently and quickly. For obvious reasons, informatization of the healthcare sector in Russia is currently experiencing an increased level of government attention (Zhilenkov & Chernyi, 2019). Financial investments in the creation of new medical technologies have a positive effect on this process and the improvement of existing services. This primarily refers to the development of unified systems, the creators of which are constantly trying to optimize the work of this software for clinics. Periodic updates provide product users with the

Table 2. Dynamics of biochemical parameters at various stages of the perioperative period

Indicator	Initial	Before Induction of Anesthesia	After Induction of Anesthesia	At the Stage of Hemostasis	On the First Day After Surgery
Glucose, mol/l	6.64±0.20	5.54±0.13	6.19±0.15	7.45±0.23	6.86±0.20
Lactate, meq/l	2.57±0.13	2.25±0.13	1.41±0.08	1.35±0.10	1.69±0.11
Creatine kinase, unit/l	60.04±3.88	80.98±5.67	82.09±6.31	103.47±8.14	294.69±38.61*
ALT, unit/l	25.82±2.41	31.58±4.90	22.98±2.79	23.55±2.81	24.84±2.82
AST, unit/l	21.26±2.28	20.82±1.47	17.94±1.30	18.77±1.37	21.56±1.51
CRP, Mg/l	1.30±0.21	3.09±0.32	1.37±0.31	1.52±0.37	19.32±2.00
Myoglobin, mcg/l	30.28±2.10	69.27±5.90	70.33±5.61	73.71±5.88	93.93±8.89**

*- p< 0.01; ** - p< 0.05

Table 3. Dynamics of hormonal status indicators at various stages of the perioperative period

Indicator	Initial	Before Induction of Anesthesia	After Induction of Anesthesia	At the Stage of Hemostasis	On the First Day After Surgery
	9.26±0.87	11.96±1.15	6.28±0.56	20.00±4.70*	11.33±1.50
ACTH, pg/ml	22.48±2.05	21.93±1.91	14.02±0.99	65.16±12.60*	21.04±2.85
Prolactin, mU/l	10.29±0.91	14.99±3.05	85.62±6.92	56.01±4.33*	10.57±1.35

*- p< 0.01

ability to use all available IT in medicine. Also in our country, an urgent need is also being fixed for the prompt implementation of effective innovations in the domestic health care system. In this regard, the issue of ensuring the most effective protection of information becomes especially important. For this reason, systems are currently being actively developed to block the threat of external intrusion to confidential medical data (Chernyi & Budnik, 2017).

CONCLUSION

Automation of local problems of the medical field allows not only helping with their solution, but also creating a systematic basis for research and forming a base of applied software of domestic production to ensure stability and high rates of rapid development.

In terms of the task being solved in the current study: according to the results of the analysis and construction of the prognostic graph, we can say that the changes in the systemic inflammatory response that occur in the body in response to direct surgical intervention on the brain were transient in nature. There was no relationship between the levels of various indicators of homeostasis and the frequency of complications in the postoperative period. Under conditions of neurovegetative stabilization with the use of fentanyl, clonidine and propofol, while maintaining the adequacy of anesthesia, a sufficient humoral response of the body to operational stress was noted. There is no "norm" for indicators of a systemic inflammatory response during surgery. There are examples of an indirect assessment of a systemic inflammatory response that are associated with catecholaminemia, which is one of the causes, and at the same time, a consequence of the development of a systemic inflammatory response. It seems interesting to further analyze these changes and compare them with the features of the clinical picture in the postoperative period, in particular, with impaired consciousness, neurodystrophic syndrome and other manifestations of the pathological organization of the central nervous system.

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