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# DYNAMICS OF PHOSPHATE LEVEL AND ADAPTATION POTENTIAL IN THE IMPLEMENTATION OF THE ERAS-PROTOCOL IN OVERWEIGHT PATIENTS WITH A SURGICAL PROFILE

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## ABSTRACT

The results of the treatment of overweight patients under the ERAS program are presented. When comparing different variants of the intensive care protocol, it is best to add colecalciferol and D-fructose-1,6-diphosphate sodium salt hydrate.

An increase in the amount of secretory active adipose tissue in the body is accompanied by a decrease in the bioavailability of vitamin D, a decrease in the level of 25 (OH) D in the blood increases the level of parathyroid hormone. The introduction of a planned surgical profile in overweight patients at the screening stage 10 days before surgery to determine the level of 25 (OH) D in the blood is a key point in deciding the possibility of a perioperative period under the ERAS program. Additional use to its classic protocol of colecalciferol (positive effect on long-term effects and is significant in the prediction process) and sodium D-fructose-1,6-diphosphate hydrate solution (directly affects the effect of rapid recovery after elective surgery) improves the quality of motor activity of patients after operations, increases their adaptive capacity by restoring lost muscle function. The optimized classical algorithm of the ERAS program significantly ( $p < 0.05$ ) improved the quality of life in the long run (30 days after surgery), such as physical functioning, general health, viability scale, mental health (SF-36 scale) and reduced body mass index.

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**Introduction.** It is known that the degree of obesity, determined by body mass index (BMI), and waist circumference are parameters associated with vitamin D3 deficiency [1]. An increase in the number of overweight people leads to an increase in the prevalence of vitamin D deficiency, which is associated with its deposition in subcutaneous fat and inaccessibility to the central bloodstream [2].

Deficiency of D-hormone leads to a decrease in the absorption of  $Ca^{2+}$  in the intestine and increase its leaching from the bones to maintain stable plasma concentrations, which is realized through the development of secondary hyperparathyroidism, increased parathyroid hormone synthesis

and the resulting activation of resorption and osteoporosis. It should be noted that the disruption of the normal functioning of the neuromuscular system may be due to a decrease in the level of D-hormone, because the conduction of nerve impulses from the motor nerves to the striated muscles and the contractility of the latter are Ca-dependent processes [3].

Also, the processes of calcium absorption and the required level of physical activity require adequate levels of vitamin D in the blood. Low serum vitamin D levels are associated with muscle weakness, increased bone fragility, and falls and fractures [4].

Vitamin D deficiency is associated with the development of diffuse muscle pain, muscle weakness, which is mainly observed in the proximal muscle group, as well as a decrease in the speed of movement. This symptomatology is due to the development of muscle atrophy, mainly muscle fibers of type II [5].

The proximal variant of muscle weakness in severe vitamin D deficiency may also be due to the development of secondary hyperparathyroidism and, accordingly, chronic hypophosphatemia [6].

Chronic hypophosphatemia can be caused by hormonal disorders, chronic diuretics, or other causes. The clinical picture depends on the time during which the depletion of phosphorus in the body, as well as the intensity of its deficiency. Chronic mild and moderate hypophosphatemia may be asymptomatic for a long time or manifested by bone pain and muscle weakness [7], altered mental status [8]. Occasionally, patients with mild hypophosphatemia may complain of weakness. In this case, it remains unclear whether the weakness is secondary to this condition, or is caused by the underlying disorder leading to the disease [9].

Since physical training and their impact on the body of a healthy person depends on the condition of muscles, including respiratory muscles, in patients after surgery, motor activity on pathogenetic changes is equated to the process of physical activity in healthy people, which is why any negative changes in the physiological state of the muscles are an obstacle to the implementation of the program of accelerated recovery after planned operations (ERAS-program).

Given that the adaptive capacity of the organism in many cases is determined by the nature and state of energy metabolism, it is of particular importance to address the issue of their optimization in determining patients with sarcopenic obesity. Thus, when determining patients at the stage of screening for vitamin D insufficiency / deficiency in the abdominal type of distribution of adipose tissue on the background of only excess body weight on the measured BMI, it is safe to say that the accumulation of fat in patients is due to reduced muscle mass. This makes it important to study their level of adaptation and energy potential at the initial level, which is directly related to the possibility of implementing the ERAS protocol.

It is known that phosphorus is involved in the formation of nucleic acids, nucleotides, phospholipids and other compounds, is involved in energy storage and transmission, in enzymatic processes, stimulates muscle contraction and is necessary to maintain the activity of neurons [10]. About 70-80% of phosphorus in the body is associated with calcium, forming the skeleton of bones and teeth, 10% is in the muscles and about 1% in the nervous tissue. The remaining part is contained in all cells of the body as a store of energy. Normally, about 1% of all phosphorus is in the blood [11]. Therefore, it was important to predict the possibility of implementing a program of accelerated recovery in patients was to determine the content of phosphates (inorganic phosphorus compounds) in the blood both at the screening stage and in the first three days of the postoperative period.

The aim of the study was to determine the adaptation potential in patients of surgical profile with excess weight in different variants of perioperative intensive care in the implementation of the ERAS protocol.

**Materials and Methods.** The basis of this study is the analysis of the results of a comprehensive clinical-instrumental and laboratory dynamic examination and evaluated the effectiveness of the proposed method of prevention and treatment in a cohort prospective randomized open clinical study in 122 patients with surgical herniological profile for a period of 1 day to 1 month after operation. Ethical aspects of the work were approved at a meeting of the commission on biomedical ethics of Kharkiv National Medical University of the Ministry of Health of Ukraine (document №8 dated 10.12.2019). All patients signed an informed consent to participate in the study.

The study was conducted by random sampling. Patients of all groups were examined before surgery in accordance with the unified clinical protocol approved by the Ministry of Health of Ukraine, which was adapted to the ERAS program. The anamnesis was carefully studied, in particular,

the postponed surgical interventions, features of the premorbid background, concomitant diseases, use of drugs. The study included patients with ventral hernias of the anterior abdominal wall, which were determined by the classification of J. P. Chevrel and A. M. Rath (SWR classification) (1999). The vast majority, 80%, had hernias of large and giant sizes), the other 20% - medium hernias.

The conditions for selecting patients for the study were age 18-60 years, increased BMI (25.0-29.9) lasting more than 10 years, the presence of primary ventral hernia, obtaining informed consent, the absence of severe metabolic and somatic acute and chronic diseases, including number of kidney diseases, absence in the anamnesis of blood diseases, oncological diseases, aggravated heredity, alcoholism, mental disorders, allergic reactions, blood transfusions, use of immunocorrectors, glucocorticoid drugs, uniformity of examination, diagnosis and preoperative preparation of the patient, condition of patients on the ASA scale - II - 100% of patients.

All patients were examined 10 days before surgery. The conditions for admission to the study under the conditions of compliance with the inclusion criteria were fences 10 days before the blood test to determine the analysis of vitamin D concentration.

Exclusion criteria were age 18 and over 60 years, consultation with an endocrinologist about hyperlicemia, consultation with a dietitian or family doctor for weight gain, daily use of medication for any comorbidities, the patient's disagreement with the study. In order to randomize patients, anesthesia and surgical treatment were considered, including the size of the hernia and the degree of degenerative changes in the abdominal wall, which can lead to complications. General characteristics of patients are shown in table 1.

Table 1. General characteristics of patients, n = 122, M ± σ

Indicator	Value
Age, years	54,2±5,9
Body weight, kg	91,6±8,9
Height, cm	175,2±12,1
IMT	28,1±1,7
Duration of anesthesia, hours	2,06±0,04
Duration of operation, hours	2,29±0,19

Patients were divided into 3 groups. Group I, control group, 32 patients hospitalized before elective surgery for primary ventral hernia, by all criteria coincided with patients of groups II and III, but did not have in the complex of perioperative intensive care additional drugs that would promote the full introduction of ERAS -program.

Group II included 44 patients who were prescribed 7,000 IU / day of vitamin D (colecalciferol 14 drops) for 10 days 10 days before the planned operation to determine vitamin D deficiency / blood concentration <30 ng / ml - day with subsequent transition to prophylactic doses - 1000 IU (2 drops/day) daily for a long period under control of body weight and vitamin D levels in the blood. The frequency of use is due to the pharmacodynamics of the drug - it is known that the maximum concentration of 25 (OH) D in serum is observed 12 hours after a single dose and returns to baseline after 72 hours. The threshold value for inclusion of the patient in the study, namely the level of 25 (OH) D in the blood <30 ng/ml, was determined on the basis of data from modern medical professional organizations [12].

Group III included 46 patients who were prescribed 7000 IU / day of colecalciferol for treatment for 10 days and then 10 days before the planned operation in terms of determining the deficiency / deficiency of vitamin D - blood concentration <30 ng / ml transition prophylactic dose - 1000 MO daily for a long period under the control of body weight and vitamin D levels in the blood. Also to the IT algorithm, patients of group III were prescribed a solution of sodium salt of D-fructose-1,6-diphosphate hydrate intravenously 150 mg / kg of ideal body weight 2 times a day at a rate of 10 ml per minute in the first 3 days of the postoperative period in the same mode introduction.

Prior to inclusion in the study, each patient received informed consent, in which the checkpoints were the day 10 days before surgery, the 1st, 2nd, 3rd day of hospital stay, as well as the possibility of an active outpatient visit (contact by phone) within 30 days after surgery. At these stages, indicators were recorded that, according to many researchers, may hinder the timely implementation of ERAS. Thirty days after surgical treatment of the primary ventral hernia, all subjects underwent an active outpatient visit (telephone call) to assess quality of life using the SF-36 questionnaire.

To determine changes in the body, to determine the level of inorganic phosphorus (phosphates) was measured by photocolorimetric method on the analyzer KFK-2MP, the reference range of 0.87 - 1.45 mmol / l.

Patients' response to surgical stress was determined, which is important for predicting the implementation of the ERAS-program. Evaluated on the basis of hemodynamic parameters - systolic blood pressure, heart rate - level of adaptation (AP) formula Baevsky RM in the modification of Bersenev AP (1987, 1997) [13]:

AP (points) = 0,011 • heart rate + 0,014 • systolic blood pressure + 0,008 • diastolic blood pressure + 0,014 • age (years) + 0,009 • body weight (kg) - 0,009 • height (cm) - 0,27.

AP ≤ 2,1 – satisfactory adaptation, AP = 2,11 – 3,2 – stress in adaptation, LA = 3,32 – 4,3 – unsatisfactory adaptation, AP > 4,3 – failure of adaptation.

Methods of parametric statistics were used to process the obtained data (Glanz S., 1999). Statistical processing of data that were entered into Excel spreadsheets was performed. The significance of the obtained data was checked using Student's t-test (for n < 100) at a given level of reliability p = 0.95. To be able to use the Student's t test, the Fischer-Snedekor test was calculated - the ratio of the larger variance to the smaller. All mathematical operations and graphical constructions were performed using the software packages "Microsoft Office XP": "Microsoft XP Home" and "Microsoft Excel XP" on a personal computer.

**Results of the research.** Since one of the main factors regulating phosphorus metabolism is parathyroid hormone, which is produced in patients with secondary vitamin D levels due to prolonged sarcopenic obesity, the possibility of implementing an accelerated recovery program in patients I, II and III can be considered by studying the dynamics of phosphorus in the blood (Table 2).

Table 2. Dynamics of blood phosphate levels in patients of groups I, II and III

Phosphate level, mmol / l	Group I n = 32	Group II n = 44	Group III n = 46
Average starting level	1,08±0,19 mmol / l		
1 day	1,10±0,22	1,20±0,26	1,42±0,08
2 day	1,10±0,21	1,19±0,24	1,42±0,09*°
3 day	1,09±0,18	1,21±0,19	1,45±0,08*°

Note: \* p < 0,05 – probable differences in relation to the average starting level;

° p < 0,05 – probable difference in relation to the figures of the control group.

When analyzing the data shown in table 2, it can be noted that at the time of screening, the average values of blood phosphates in all patients were in the range of control values, with the minimum values of this indicator in groups I, II and III was 0.91 mmol / l, 0.89 mmol / l and 0.87 mmol / l, and the maximum - 1.25 mmol / l, 1.29 mmol / l and 1.25 mmol / l, respectively, the average initial concentration was 1.08 ± 0.19 mmol / l.

Subsequently, in group I during the first three days of intensive care according to the classical program of accelerated recovery for patients with primary ventral hernias, the indicators of this indicator did not differ from the screening and were 1.10 ± 0.22 mmol / l, 1.10 ± 0.21 mmol / l and 1.09 ± 0.18 mmol / l on the 1st, 2nd f-th day of treatment, respectively. Given the dynamics of phosphatemia in patients in this group, it can be concluded that surgery, anesthesia and perioperative therapy alone do not affect phosphorus metabolism in the body.

In turn, in subjects of group II on the 1st day of hospital stay the level of phosphate in the blood serum was 1.1 ± 0.26 mmol / l, which was 10% higher than at the screening stage and in patients I groups. on the 2nd and 3rd day of hospital stay the dynamics of this indicator was the same and its indicators were 1.19 ± 0.24 mmol / l and 1.21 ± 0.19 mmol / l, respectively. In this case, a larger difference was found between the min-max digits of the studied marker compared with group I.

A completely different clinical and diagnostic picture was observed in patients of group III. Thus, on the first day of intensive care, the concentration of phosphates in the blood was 1.42 ± 0.13 mmol / l, which was 24% higher than the indicators of phostatemia at the screening stage and on day 1 of treatment in patients of group I.

Subsequently, on the 2nd and 3rd days of hospital stay, the serum phosphate concentration was 1.42 ± 0.09 mmol / l and 1.45 ± 0.08 mmol / l, which is probably (p < 0.05) exceeded the average baseline level and probably (p < 0.05) exceeds the level of this indicator daily in group I.



When comparing the dynamics of phosphatemia in the studied groups II and III, the average values were exceeded by 20%, and if in group II no patient was determined by the number of phosphate levels in the blood, which would be in the upper limit of reference values, ie 1,45 mmol / l , in contrast, in group III in 30% of patients blood phosphates exceeded the upper limit of normal values.

Thus, it can be concluded that additional administration of colecalciferol to overweight patients lasting more than 10 years with preoperative screening deficiency / vitamin D deficiency has a positive effect on phosphate metabolism in the body and additional phosphate donor administration makes it more stable and long-lasting.

Given the fact that the total need for phosphate cannot be predicted by serum levels due to the fact that phosphate moves between many parts of the body, the concentration of total phosphorus consists of inorganic phosphorus (phosphates) and phosphorus basic organophosphorus compounds, and given the presence of subjects preliminary data on the possible development of sarcopenic obesity, it is important to determine the energy potential of cells and the level of adaptation, which is a general criterion for the interaction of energy potential and functionality of the patient. To do this, we studied the level of adaptation in patients of groups I, II and III on the 1st, 2nd and 3rd days of intensive care by calculating the adaptive potential of the organism by the method of Baevsky RM in modification Bersenev AP (1997) (table 3).

Table 3. Adaptive potential in patients of groups I, II and III  
 $AP \leq 2,1$  – satisfactory adaptation,  $AP = 2,11 - 3,2$  – stress in adaptation,  $LA = 3,32 - 4,3$  – unsatisfactory adaptation,  $AP > 4,3$  – failure of adaptation.

Characteristics of adaptation	Group I, n = 32			The entire postoperative period
	1 day	2 day	2 day	
<2 – satisfactory adaptation	8 (25%) patients 1,9±0,2	8 (25%) patients 1,98±0,1	14 (44%) patients 1,96±0,1	<b>2,96±0,2</b>
2,1 – 3,2 – stress in adaptation	10 (31%) patients 2,78±0,4	10 (31%) patients 2,97±0,2	10 (31%) patients 3,1±0,1	
3,21-4,3 – unsatisfactory adaptation	14 (44%) patients 3,98±0,3	14 (44%) patients 4,1±0,2	8 (25%) patients 3,92±0,2	
>4,3 failure of adaptation	0	0	0	
Characteristics of adaptation	Group II, n = 44			The entire postoperative period
	1 day	2 day	2 day	
<2 – satisfactory adaptation	20 (45%) patients	20 (45%) patients	18 (41%) patients	<b>2,75±0,2</b>
2,1 – 3,2 – stress in adaptation	10 (23%) patients	14 (32%) patients	18 (41%) patients	
3,21-4,3 – unsatisfactory adaptation	14 (32%) patients	10 (23%) patients	8 (18%) patients	
>4,3 failure of adaptation	0	0	0	
Characteristics of adaptation	Group III, n = 46			The entire postoperative period
	1 day	2 day	2 day	
<2 – satisfactory adaptation	26 (57%) patients 1,82±0,04	40 (87%) patients 1,74±0,06	42 (91%) patients 1,71±0,02	<b>2,17±0,07*</b>
2,1 – 3,2 – stress in adaptation	14 (30%) patients 2,4±0,09	6 (13%) patients 2,3±0,1	4 (9%) patients 2,3±0,18	
3,21-4,3 – unsatisfactory adaptation	6 (13%) patients 3,28±0,07	0	0	
>4,3 failure of adaptation	0	0	0	

Note: \*  $p < 0,05$  – probable difference in relation to the general indicator of adaptive potential of groups I and II.

In the analysis of data obtained in determining the adaptation potential of patients of groups I, II and III during the 1st, 2nd and 3rd days of the postoperative period, the probable ( $p < 0,05$ ) relationships between the ability of patients to perform ERAS- program and components of intensive care.

Thus, when calculating the total number of points of adaptation potential for the entire observation period in patients of group III was found a probable ( $p < 0,05$ ) difference from groups I and II, while between groups I and II there was no statistically significant difference, their total scores were  $2.96 \pm 0.2$  points and  $2.75 \pm 0.2$  points, respectively, indicating adaptation stress in patients in these groups throughout the follow-up period. In contrast, in group III, the overall indicators of this indicator were  $2.17 \pm 0.07$  points, which was defined as satisfactory adaptation.

Analyzing the percentage of patients in group I with the appropriate number of points that characterize the adaptation as satisfactory / stressful / unsatisfactory, it can be noted that the first 48 hours of the postoperative period, internal redistribution by type of potential did not differ and was determined by 25% / 31% / 44% of patients. general description as "adaptation stress". On the 3rd day of intensive care, the redistribution of satisfactory / stress / unsatisfactory was slightly better, 44% / 31% / 25%, but in general in the study during the entire observation period the adaptive potential of the whole group as a general indicator of patients was at the level of stress. adaptive capabilities of the organism.

Analyzing the percentage of patients in group II with the appropriate number of points that characterize the adaptation as satisfactory / stressful / unsatisfactory, it can be noted that on the first day of treatment, when the distribution was 45% / 23% / 32%, almost 1/3 of patients had unsatisfactory adaptability, however, in contrast to group I (25%), satisfactory adaptation of the organism was determined in 45% of them. On days 2 and 3, hospital stays were positive only between stress / unsatisfactory performance, which was 32% and 23% and 41% and 18%, respectively. The overall adaptive potential of the whole group as a total indicator of patients was at the level of stress adaptive capacity of the organism throughout the observation period.

The percentage of patients of group III in the form of sharply positive dynamics of its indicators every following day of intensive care was interesting. Thus, on the 1st day of treatment the ratio of adaptive characteristics as satisfactory / stress / unsatisfactory was in 135, 30% and 57% of patients, respectively, on the 2nd day - 0%, 13% and 87%, on the 3rd - 0 %, 9% and 91% of subjects. Given that in this group of patients the overall indicators of adaptation potential  $2.17 \pm 0.07$  points were probably ( $p < 0.05$ ) lower than in groups I and II against the background of relatively small differences between the indicators in the range of variations of patients daily , we can argue about the most successful of the proposed options for perioperative therapy, which undoubtedly contributes to the implementation of the program of accelerated recovery and can be used in everyday practice.

**Discussion of results.** Important is the fact that a significant element that promotes accelerated recovery in the postoperative period in the presence of sarcopenic obesity in the patient is the level of phosphatemia, which is indirectly a possible factor in predicting the energy potential of body cells. Additional administration of phosphate-containing drugs during the period when the patient needs to exercise, including during the introduction of ERAS-protocol in overweight patients after elective surgery, in which screening determines vitamin D deficiency / deficiency, is an important element of the patient's treatment algorithm. violation of the content of vitamin D causes metabolic changes, which in 100% of cases involve a violation of phosphorus metabolism in the body. It can also be predicted that the additional introduction of a phosphate source operates on the principle of feedback, ie increasing the level of phosphate in the blood reduces the secretion of parathyroid hormone.

### **Conclusions.**

1. Based on current data, metabolic changes in the body, which are caused by the influence of the secretory function of adipose tissue as an independent endocrine organ, have a significant impact on the prognosis of the postoperative period. In patients with a surgical profile of overweight lasting more than 10 years, it is important to determine the level of vitamin D, phosphorus and calculate adaptive capabilities when planning patient management tactics after elective surgery, which directly affects the possibility of ERAS implementation and quality of life as remote treatment prognosis.

2. An increase in the amount of secretory active adipose tissue in the body is accompanied by a decrease in the bioavailability of vitamin D, a decrease in the level of 25 (OH) D in the blood increases the level of parathyroid hormone. The introduction of a planned surgical profile in overweight patients at the screening stage 10 days before surgery to determine the level of 25 (OH) D in the blood is a key point in deciding the possibility of a perioperative period under the ERAS

program. Additional use to its classic protocol of colecalciferol (positive effect on long-term effects and is significant in the prediction process) and sodium D-fructose-1,6-diphosphate hydrate solution (directly affects the effect of rapid recovery after elective surgery) improves the quality of motor activity of patients after operations, increases their adaptive capacity by restoring lost muscle function.

**Conflict of interest.** The authors do not declare a conflict of interest.

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