

Perioperative Changes in Hemodynamics and its Connection with Serum Levels of Cholesterol and Triglycerides in Patients who Endured Laparoscopic and Conventional Surgery

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Abstract: *The endocrine system plays an important role in the homeostasis of the body securing the interrelation between the cells, the tissues and the organs. A number of adverse reactions for the body originate during anesthesia, pain or surgical trauma (nervous-endocrine, immunological, psychological and so on), characterized by the release of hormones as cortisol, adrenocorticotrophic hormone, thyroid-stimulating hormone as well as of their precursors – cholesterol and so on. This hormonal "explosion" in the system blood circulation provokes hemodynamic changes, which may be exceptionally adverse for the patients especially in the course of the anesthesia or the surgical trauma.*

Keywords: cholesterol, triglycerides, hemodynamics, anesthesia.

1. Introduction

It is known that all the glands with internal and external secretion are functionally connected with each other. Great importance is, however, attached to some of the glands with internal secretion, in the anesthetic and the surgical activities in view to the surgical stress arising in the course of the operative intervention, as well as to a number of nervous structures in the central nervous system – the pituitary gland, the hypothalamus and so on.

The reason for this is that they exert direct and indirect impact over a lot of organs and systems and mediate the development of some adverse moments concerning predominantly the cardiovascular system.

Any trauma – irrespective of its nature – surgical interference or a traumatic incident, activates a nervous-endocrine response, which frequently results in complications in the intraoperative and the early postoperative period.

The anesthetic medicaments, the complicated surgical procedures and the pre-operative condition of the patients are in a position to increase the operative risk. (1)

Thanks to the multitude of researches conducted in the last few years, the connection between the operative stress and the changes occurring in the vital indicators in the course of anesthesia was proven in an indisputable manner.

Not only the widely applied at the moment conventional surgical techniques but the laparoscopic such start to be used more and more frequently due to their small trauma.

The steroid hormones are attached a significant role in the development of the "stress-surgical response" during

surgical operative interferences, whose precursor cholesterol is, irrespective of their type.

Each cell in the body of mammals contains cholesterol. It is in the membranes of the cells. It participates in the synthesis of the hormones, the hormones of the adrenal gland and so on.

2. Objective

To establish the dynamics of the serum levels of cholesterol, triglycerides and hemodynamic indicators Systolic Arterial Pressure, Diastolic Arterial Pressure and Heartbeat in patients operated through a laparoscopic and a conventional surgical method.

3. Materials and Methods

3.1 Clinical Contingent

The tested clinical contingent comprises 80 patients treated in the University Multi-Profile Active Treatment Hospital "Sveta Marina" – town of Pleven during the period 2018, of whom 7 (8,8%) men and 73 (91,3%) women (Fig. 1). The average age of the participants in the research is $50,40 \pm 12,41$ years within the interval between 18 and 79 years old.

It is seen from Fig. 2 that the biggest number (6) for men is from age group 60-69 years old, followed by 70-79 years old by 1. There are no men in the lower age groups.

For women the biggest number (25) is from age group 40-49 years old followed by 50-59 by 22. The smallest number (1) is from age group 10-19 years old.

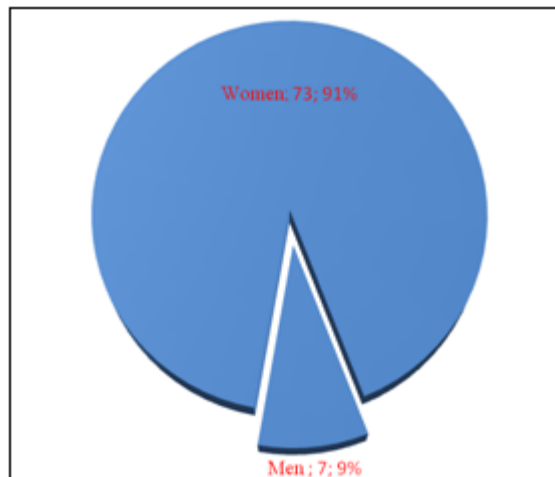


Figure 1: Frequency distribution of the investigated contingent with regard to gender belonging

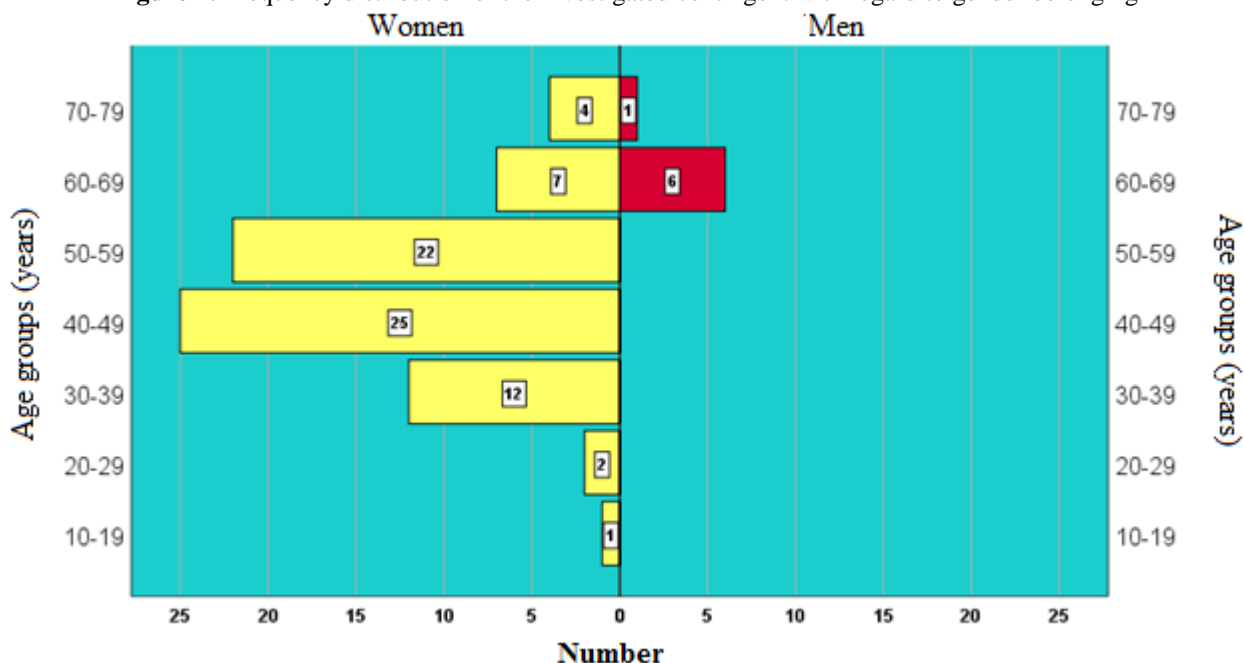


Figure 2: Distribution of the investigated belonging per gender and age groups

Laboratory Methods

The serum values of the total cholesterol and the triglycerides in five consecutive stages were investigated for all the patients: on the day prior to the operative interference, during the interference, directly after the admission of the patient into reanimation, on the first and the second postoperative days. The tests were made in the Clinical Laboratory of the University Multi-Profile Active Treatment Hospital “Sveta Marina” – town of Pleven.

Clinical Methods

The values of the Systolic Arterial Pressure, the Diastolic Arterial Pressure, the Average Arterial Pressure and the Heartbeat were reported in nine consecutive moments (output values, after the premedication, after the intubation, at the beginning of the operation, on the 15th minute after the operation, on the 30th minute after the operation, during the traumatic moment, at the end of the operation and after the extubation).

Statistical Methods

The data were entered and processed with the statistical package IBM SPSS Statistics 25.0. p<0.05 was accepted as level of significance at which the zero hypothesis is rejected.

4. Results

The participants in the research were divided into two diagnostic groups:

- Group 1 – patients who underwent through a laparoscopic operation (n=40);
- Group 2 – patients with performed an open (conventional) operation (n=40).

It was proven that the patients from the entire extract have normal frequency distribution with regard to the indicators age, weight, Body Index and other than the normal pertaining to the indicator height (Fig. 3).

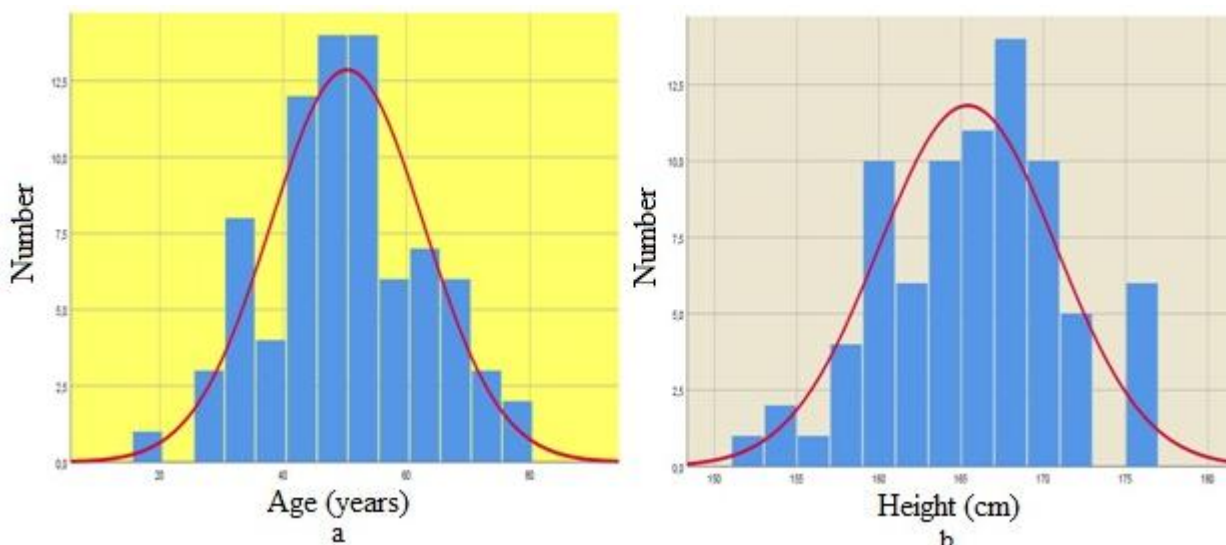


Figure 3: Frequency distribution of the patients from the entire extract with regard to: a/ age, $p=0,200$; b/ height, $p=0,017$; c/ weight, $p=0,200$; d/ Body Mass Index, $p=0,06$

Number Number
Weight (kg) IBW (kg/m²)

The diagnosis with the biggest relative share (23,8%) is uterine fibroids followed by carcinoma of the cervix by 21,3%, (Table 1).

Table 1: Frequency distribution of the patients per diagnosis

Diagnosis	Number	%	Sp
Uterine Fibroids	19	23,8	4.8
Carcinoma of Cervix	17	21,3	4.6
Ovarian Cyst	13	16,3	4.1
Ovarian Cancer	5	6,3	2.7
Acute cholecystitis	5	6,3	2.7
Breast Cancer	4	5,0	2.4
Mechanical ileus	4	5,0	2.4
Kidney tumor	2	2,5	1.7
Lung Cancer	2	2,5	1.7
Rectum carcinoma	1	1,3	1.2
Bladder Carcinoma	1	1,3	1.2
Kidney hydronephrosis	1	1,3	1.2
Pleural Effusion	1	1,3	1.2
Endometrial carcinoma	1	1,3	1.2
Dehydration of the vagina	1	1,3	1.2
Tubo-ovarian abscess	1	1,3	1.2
Hiatal hernia	1	1,3	1.2
Endometriosis of the rectovaginal sinus	1	1,3	1.2
Total	80	100,0	

Two of the diagnoses are with single representativeness, due to which they get within the aggregated group "Other Diseases", which the following refer to: Rectum carcinoma, Bladder carcinoma, Kidney hydronephrosis, Pleural effusion, Endometrial carcinoma, Dehydration of the vagina, Tubo-ovarian abscess, Hiatal hernia, Endometriosis of the rectovaginal sinus. The results from Table 2 indicate that the aggregated group of patients with "Other Diseases" is with the biggest relative share (50,0%) from the accompanying diseases, followed by the patients with cardiovascular diseases (CVD) by 48,8%, and the diseases of the musculoskeletal system are with the smallest representativeness (two or 2,5%).

Table 2: Frequency distribution of the patients with regard to accompanying diseases

Accompanying Diseases	Number	%	Sp
Other diseases	40	50,0	5,6
Cardiovascular diseases	39	48,8	5,6
Blood diseases	21	26,3	4,9
No Accompanying diseases	15	18,8	4,4
Endocrine diseases	11	13,8	3,9
Respiratory system diseases	9	11,3	3,5
Kidney diseases	9	11,3	3,5
Nervous system diseases	5	6,3	2,7
Musculoskeletal system diseases	2	2,5	1,7

It was important for the needs of the research to seek the availability of connection between the changes in the serum levels of the cholesterol with regard to the hemodynamic indicators (Systolic Arterial Pressure, Diastolic Arterial Pressure, Average Arterial Pressure and Heartbeat) in the two investigated groups of patients.

The results from tables 3 and 4 indicate that the cholesterol and the Systolic Arterial Pressure for patients with a laparoscopic operation do not correlate in any of the times of measurement whilst for patients with an open operation correlation is established solely between the pre-operative value of the cholesterol and the Systolic Arterial Pressure at the end of the operation. The dependence is moderate in force and inversely proportional.

In the laparoscopic group the postoperative cholesterol correlates moderately and inversely proportionally with the measured Diastolic Arterial Pressure **15 min. after the beginning of the operation**;

In the group of the patients with performed open operation the intra-operative cholesterol indicates a moderate and in direct ratio connection with the measured Diastolic Arterial Pressure after the intubation and after the extubation, and the postoperative cholesterol – moderately and in direct ratio to the measured Diastolic Arterial Pressure **15 min. after the**

beginning of the operation and after the extubation (Tables 5 and 6).

In patients with a laparoscopic operation the intra-operative cholesterol correlated moderately and inversely proportionally with the measured Average Arterial Pressure at the beginning of the operation, whilst in patients with an open operation the postoperative cholesterol correlates moderately and in direct ratio to the measured Average Arterial Pressure after the extubation (Tables 7 and 8).

It makes impression that no activities of correlation between the values of the cholesterol and the heartbeat at any of the

times of measurement are established in patients with a laparoscopic operation;

In patients with an open operation the pre-operative cholesterol correlates moderately and in direct ratio to the measured heartbeat 30 min. after the beginning of the operation and after the extubation, and the postoperative - moderately and in direct ratio to the measured heartbeat 30 min. after the beginning of the operation, at the end of the operation and after the extubation (Table 9 and Table 10).

Table 3: Correlation analysis between the levels of the total cholesterol and the Systolic Arterial Pressure at the various times of measurement, laparoscopic operation

Indicators	Cholesterol				
	Systolic Arterial Pressure	Pre-operative	Intraoperative	Postoperative	First postoperative day
Output		0,154	0,104	0,154	0,185
After the premedication		0,020	-0,025	0,056	0,191
After the intubation		-0,081	-0,117	-0,070	0,041
At the beginning of the operation		-0,104	-0,183	-0,100	-0,037
15 min. after the beginning of the operation		-0,065	-0,065	-0,133	0,049
30 min. after the beginning of the operation		-0,051	-0,072	-0,091	-0,021
During the traumatic moment		-0,053	-0,068	-0,099	-0,041
At the end of the operation		0,020	-0,010	-0,074	-0,018
After the extubation		-0,138	-0,119	-0,094	0,065

* p<0,05, ** p<0,01, *** p<0,001

Table 4: Correlation analysis between the levels of the total cholesterol and the Systolic Arterial Pressure at the various times of measurement, open operation

Indicators	Cholesterol				
	Systolic Arterial Pressure	Pre-operative	Intraoperative	Postoperative	First postoperative day
Output		-0,106	-0,033	0,031	0,042
After the premedication		-0,170	-0,089	-0,047	-0,027
After the intubation		-0,016	0,069	0,108	0,027
At the beginning of the operation		-0,206	-0,099	0,005	-0,112
15 min. after the beginning of the operation		-0,078	-0,084	0,138	0,024
30 min. after the beginning of the operation		0,009	0,037	0,107	0,204
During the traumatic moment		-0,297	-0,124	-0,139	-0,165
At the end of the operation		-0,384*	-0,220	-0,256	-0,173
After the extubation		-0,027	0,120	0,181	0,101

* p<0,05, ** p<0,01, *** p<0,001

Table 5: Correlation analysis between the levels of the total cholesterol and the Diastolic Arterial Pressure at the various times of measurement, laparoscopic operation

Indicators	Cholesterol				
	Diastolic Arterial Pressure	Pre-operative	Intraoperative	Postoperative	First postoperative day
Output		0,040	-0,033	0,021	0,070
After the premedication		0,014	-0,098	0,056	0,175
After the intubation		-0,108	-0,149	-0,074	0,069
At the beginning of the operation		-0,140	-0,218	-0,164	-0,122
15 min. after the beginning of the operation		-0,288	-0,266	-0,375*	-0,197
30 min. after the beginning of the operation		-0,217	-0,225	-0,146	-0,104
During the traumatic moment		-0,216	-0,219	-0,131	-0,075
At the end of the operation		0,086	0,012	0,036	0,193
After the extubation		0,042	0,087	0,168	0,178

* p<0,05, ** p<0,01, *** p<0,001

Table 6: Correlation analysis between the levels of the total cholesterol and the Diastolic Arterial Pressure at the various times of measurement, open operation

Indicators	Cholesterol				
	Diastolic Arterial Pressure	Pre-operative	Intraoperative	Postoperative	First postoperative day
Output		0,074	0,029	0,054	-0,078
After the premedication		-0,065	0,077	-0,051	-0,072

After the intubation	0,275	0,370*	0,259	0,223
At the beginning of the operation	-0,274	-0,124	-0,221	0,014
15 min. after the beginning of the operation	0,252	0,136	0,335*	0,222
30 min. after the beginning of the operation	0,283	0,257	0,237	0,197
During the traumatic moment	-0,011	-0,117	-0,092	-0,115
At the end of the operation	0,060	0,127	0,026	0,182
After the extubation	0,154	0,336*	0,371*	0,139

* p<0,05, ** p<0,01, *** p<0,001

Table 7: Correlation analysis between the levels of the total cholesterol and the Average Arterial Pressure at the various times of measurement, laparoscopic operation

Indicators	Cholesterol			
	Pre-operative	Intraoperative	Postoperative	First postoperative day
Average arterial pressure				
Output	0,053	-0,013	0,057	0,142
After the premedication	0,011	-0,072	0,058	0,204
After the intubation	-0,094	-0,139	-0,074	0,064
At the beginning of the operation	-0,295	-0,332*	-0,294	-0,257
15 min. after the beginning of the operation	-0,196	-0,186	-0,280	-0,086
30 min. after the beginning of the operation	-0,162	-0,172	-0,137	-0,060
During the traumatic moment	0,009	-0,050	0,010	0,127
At the end of the operation	0,080	0,022	0,009	0,111
After the extubation	-0,051	-0,013	0,046	0,152

* p<0,05, ** p<0,01, *** p<0,001

Table 8: Correlation analysis between the levels of the total cholesterol and the Average Arterial Pressure at the various times of measurement, open operation

Indicators	Cholesterol			
	Pre-operative	Intraoperative	Postoperative	First postoperative day
Average arterial pressure				
Output	-0,054	-0,028	0,087	-0,025
After the premedication	-0,128	0,020	0,028	0,007
After the intubation	0,136	0,244	0,234	0,156
At the beginning of the operation	-0,235	-0,087	-0,049	-0,023
15 min. after the beginning of the operation	0,087	0,041	0,283	0,149
30 min. after the beginning of the operation	0,191	0,200	0,253	0,265
During the traumatic moment	-0,189	-0,108	-0,063	-0,099
At the end of the operation	-0,177	-0,035	-0,076	0,037
After the extubation	0,074	0,264	0,351*	0,174

* p<0,05, ** p<0,01, *** p<0,001

Table 9: Correlation analysis between the levels of the total cholesterol and the Heartbeat at the various times of measurement, laparoscopic operation

Indicators	Cholesterol			
	Pre-operative	Intraoperative	Postoperative	First postoperative day
Heartbeat				
Output	0,051	-0,053	-0,035	-0,214
After the premedication	0,055	-0,038	-0,024	-0,214
After the intubation	-0,015	-0,116	-0,086	-0,257
At the beginning of the operation	0,141	0,029	0,021	-0,113
15 min. after the beginning of the operation	-0,007	-0,098	-0,172	-0,248
30 min. after the beginning of the operation	-0,022	-0,092	-0,131	-0,211
During the traumatic moment	0,004	-0,068	-0,049	-0,029
At the end of the operation	-0,014	-0,069	-0,142	-0,186
After the extubation	-0,093	-0,094	-0,131	-0,152

* p<0,05, ** p<0,01, *** p<0,001

Table 10: Correlation analysis between the levels of the total cholesterol and the Heartbeat at the various times of measurement, open operation

Indicators	Cholesterol			
	Pre-operative	Intraoperative	Postoperative	First postoperative day
Heartbeat				
Output	0,169	0,174	0,165	0,013
After the premedication	0,197	0,193	0,203	0,023
After the intubation	0,250	0,309	0,241	0,042
At the beginning of the operation	0,107	0,076	0,147	-0,024
15 min. after the beginning of the operation	0,179	0,190	0,181	-0,011
30 min. after the beginning of the operation	0,416**	0,300	0,359*	0,197
During the traumatic moment	0,139	0,066	0,221	0,059
At the end of the operation	0,287	0,284	0,312*	0,264

After the extubation	0,350*	0,279	0,334*	0,266
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* p<0,05, ** p<0,01, *** p<0,001

5. Discussion

The activation of the sympathetic nervous system, the increase of the catabolic hormone secretion and the suppression of the pituitary gland are deemed as a reaction of the surgical stress. In the clinical practice this results in a change in the heartbeat, the arterial blood pressure and biochemical oscillations of noradrenalin, adrenalin, dopamine and cortisol. (13), (6)

Adams and colleagues announce that the most significant factors determining the level of stress-reaction are the patient, the type of the anesthesia and the operation. According to this author's team anesthesia may change the stress response through afferent blockade (local anesthesia), central modulation (general anesthesia) and peripheral interaction with the endocrine system (etomidate). (1), (8), (3)

According to Desborough (2000) and Kehlet (2006), the "high-dosage" opiate anesthesia or the administration of volatile agents with high minimal values of the maximal alveolar concentration (MAC), suppress the intra-operative endocrine-metabolite response to the operation but without permanent effect over the postoperative responses and the nitrogen balance. (1), (9)

According to other authors, even with sufficiently deep anesthesia the surgical stimulus results in hormonal and metabolite changes provoking the release of hormones from the frontal part of the hypothalamus. (3)

No doubt, however, the type of the surgical interference and anesthesia exert substantial impact over the hemodynamics of the patient in the intra-operative period.

Huiku M. and colleagues (2007) prove that the chest and gynecological operations result in hemodynamic changes during the surgical section. In this research the hemodynamic variables were higher than the output level after the beginning of the operation. (7), (15)

We established in the research conducted by us that the values of the hemodynamic indicators Systolic Arterial Pressure, Diastolic Arterial Pressure, Average Arterial Pressure and Heartbeat in the course of the anesthesia and the operative interference show a tendency to decrease during the entire operation. There is a tendency to their increase solely during the traumatic moment and the beginning of the operative interference and after the suspension of the supply of anesthetics at the end of the anesthesia, which confirms the results of the author's collective teams indicated hereinabove.

It is admitted that the minimally-invasive surgical operations (laparoscopic and robotized), result in weaker reaction of stress for the patient.

Insufflation in the abdominal cavity of CO₂ or other gases exerts impact over the reaction of metabolism. CO₂

insufflation may provoke both local and systematic reactions which affect the metabolic response during an operation. According to Thorell A. metabolic response is more seldom encountered in the minimally invasive surgery. (15)

Carli and colleagues identify similar assertions at laparoscopic segmental colectomy. (2)

Laparoscopic hysterectomy results in smaller and shorter increase of IL6 and CRP as compared to open surgery. This is why it causes smaller tissue trauma and more weakly expressed inflammatory reaction. The synthesis of cytokines from the mesothelial cells is smaller after laparoscopy as compared to the open surgery. (10)

With regard to metabolic changes during an operation, according to some authors, surgical trauma does not exert significant impact over the energy metabolism in older people. (12)

Cuthbertson and colleagues announce about 20-25% increase of the metabolic speed after trauma and announce that the size of the metabolic response is related to the seriousness of the trauma. (12)

The changes in the metabolism are related to the changes in the temperature of the heart and the heartbeat. The increase of the energy metabolism during the postoperative period is confirmed by many recent researches. It is established that metabolism increases by 15-30%. Cuthbertson also proves that the postoperative response may be changed by changes made during the conducted pre-operative and postoperative treatment. (12)

The postoperative changes in the energy metabolism, the thermal regulation and the needs of liquids and energy vary amongst newborns, children and older people. (12)

According to other scientists, however, surgical interference affects the metabolism and the use of substrates as glucose at any age. After an operation, the use of glucose decreases due to insulin resistance with the increase of the triglycerides and the decomposition of the free fatty acids due to the increase of the secretion of the catecholamines. (5), (2)

The disturbed lipid exchange in stress may be determined by an ensemble of hormones, main components of which the glucocorticoids are.

Cholesterol is used for the synthesis of glucocorticoids.

In extreme conditions, the quantity of cholesterol in the adrenals may turn out to be insufficient which contributes to increased supply of cholesterol with the fraction of lipoproteins with low density.

At that, the level of lipoproteins with high density simultaneously increases.

It is established that the free fatty acids are primary sources of energy after trauma.

It is proven that triglycerides provide 50-80% of the consumed energy after trauma and critical diseases. The energy needed for the increased gluconeogenesis is provided by lactate or amino acids in the liver. Lipolysis accelerates in the early period due to the increased levels of ACTH, cortisol, catecholamine, glucagon, growth hormone and insulin and reduced sympathetic activity. (14)

Irrespective of etiology, the increased degree of the lipolysis is an expected condition within the framework of the metabolic reactions in critically ill patients irrespective of the fact that the quantity of fatty acids as a result of the lipolysis may exceed the energy needs. (14)

We proved in the research conducted by us that the level of cholesterol and triglycerides in patients subjected to planned laparoscopic and conventional operative intervention are with a tendency towards decrease intra-operatively and on the first postoperative day with regard to the pre-operative values.

Inversely proportional correlation was reported in the conventional group solely between the pre-operative value of the cholesterol with Diastolic Arterial Pressure and Systolic Arterial Pressure at the end of the operation and with Diastolic Arterial Pressure after the intubation and the extubation.

Such a connection was found out in the laparoscopic group only between the cholesterol and the Diastolic Arterial Pressure on the 15th minute after the beginning of the operation.

In both groups (conventional and laparoscopic), the Average Arterial Pressure indicates a direct ratio correlation connection with the triglycerides at each stage of the research.

Age as an indicator correlates in direct ratio to the Systolic Arterial Pressure, the Diastolic Arterial Pressure and the operative time.

We established that in patients who suffered trauma, the values of cortisol are the highest on the day of the trauma and on the fourth day after the operative intervention (during the early movement and rehabilitation).

The cholesterol also shows tendency to increase during the traumatic moment, and its values decrease in parallel with those of cortisol on the 2nd and the 3rd postoperative day.

The triglycerides are with a tendency to permanent increase during all the days of the research.

The operative time shows dependence solely with regard to the level of cortisol, the more continuous the operative interference is, the higher the percentage with high levels of cortisol on the 3rd and the 7th day after the operation is.

Women are with higher levels of cortisol and cholesterol as compared to men and this dependence does not show any connection with the accompanying diseases in both genders.

Solely the serum levels of the triglycerides turn out with higher values in patients with accompanying pathology.

The conclusion may be drawn on the basis of the results obtained that in patients who suffered trauma (incident or operative interference), a number of hemodynamic changes related to the high levels of catecholamines, in particular of cortisol, is observed.

The accompanying diseases, the age, the operative and anesthesiologic time exert relatively weaker impact over the changes observed (the serum levels of cholesterol, triglycerides, some hemodynamic indicators and so on) in the course of anesthesia, perhaps owing to the impact of the medicaments used in the course of the general anesthesia.

6. Conclusion

Surgical trauma, anesthesiology, pain and others are in a position to provoke a number of adverse reactions for the body (nervous-endocrine, immunological, psychological and so on).

This causes the release of a multitude of hormones (cortisol, ACTH, TSH and so on) and interleukins, as well as changes in the levels of the serum cholesterol and triglycerides, which provoke both physiological and pathophysiological reactions in the human body.

This may turn out to be extremely unfavorable, in particular in patients with accompanying diseases.

The properly selected type of anesthesia and applied anesthetic medicaments may play a key role for the reduction of the nervous-endocrine response in trauma.

The knowledge of the changes which occur during "stress" (operative trauma or traumatic incident), as well as the possibility in these events to apply minimally-invasive surgical methods combined with the appropriate type of anesthesia are in the basis of the favorable outcome from the performed operative interference in the conditions of intense stress-hormonal reaction.

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