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Research Article

Relation between Neurohumoral Feedback to Surgical - Anaesthetic Aggression and Vegetative Nervous System Type

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Abstract

The article was dedicated to the study of neurohumoral changes occurring during combined endotracheal epidural anesthesia (CEEA) applied in large-scale surgical operations on abdominal cavity organs and defining the dependence of hormonal state dynamics on vegetative nervous system type.

The scientific research was conducted on 69 patients who underwent large scale surgical operations in Anaesthesiology - Reanimation Department of SSC named after acad. M.A. Topchubashev due to different serious abdominal pathologies in years 2007 - 2014. Electroencephalography, Cerdo Vegetative Index, Hildebrandt coefficient and single neurophysiological tests were used to determine VNS type. The patients were divided into three groups depending on vegetative nervous system type: I - normotonics- 17 patients (24,7%), II - sympathatonics- 25 patients (36,2%), and III - vagotonics- 27 patients (39,1%). Blood adrenocorticotropic hormone (ACTH) and cortisol (Cs) concentration were studied in 3 stages: I - preoperative, II -operation traumatic stage, III - the 1st postoperative day.

The obtained results displayed that the number of stressor hormones in every three groups increased statistically certain in aggressive stage of surgical operation and later, that is within the III stage approached the initial level. The level of stressor hormones remained statistically certain increased as compared with initial indexes only in sympathatonics in comparison with normotonics and vagotonics in the III stage. This is explained by higher level of sympathomimetic state in sympathatonics in comparison with the other groups.

Keywords: *Vegetative Nervous System Type; Combined Endotracheal Epidural Anesthesia; Abdominal Surgery*

Introduction

Some advantages specific to combined endotracheal epidural anesthesia (CEEA) have recently led to its application by anesthesiologists in the anesthesiological provision of large-scale and very traumatic surgical operations of abdominal organs. CEEA distinguished for properties and features of the clinical course is a protective anesthesia option providing adequacy during operations [1-4]. Overdose or under dose of anesthesia medications applied in general anesthesia may lead to functional disorders resulting in certain postoperative complications of the vegetative nervous system (VNS) [5,6].

The nature of the VNS response to the operational trauma and pharmaceutical aggression depends on its predominating part [7-9]. In addition to main impacts of the general anesthesia on functions of organs and systems, as well as the impact of anesthesia medications on the central nervous system (ataraxia, neuroleption, analgesia, anesthesia etc.), there are also side effects. These effects develop as sympathetic and parasympathetic tonus changes, ganglionary blockage, energetic and temperature imbalance [9-11].

Effects of anesthetics on the neurohumoral regulation of the cardio-vascular system (CVS) depend on the various variants of the vegetative homeostasis, prevalence of its sympathomimetic and vagotonic properties [7,9,12]. Course of general anesthesia depends on the state of the vegetative homeostasis [7,10,11]. Records of certain VNS and homeostasis indicators in the anesthetic card reflect these properties [4,12]. Medications used in anesthesia, as well as pain stimulation and the disease itself usually create side effects which are mainly evident through VSS indicators [3,5,7,10].

Homeostasis is provided through stable functioning of all organs under the influence of both sympathetic and parasympathetic nervous system. Both systems function within the close interaction [9-11]. However, there may arise cases of functional prevalence of one system over the other one. Cases of high tonus of a parasympathetic part is called parasympathotony or vagotony, and high tonus of the sympathetic system is called sympathotony. Cases when neither of the systems prevails are assessed as normotony [9]. Connection of demand of analgetic and other components in the adequate anesthesiologic provision of surgical operations with the activity of the opioid system is not under question [9-11].

Purpose

Purpose of the work was to study the relation of the neurohumoral response of an organism against surgical and anesthesiologic aggression during large-scale operations performed with CIEA with the type of the vegetative nervous system.

Materials and Methods

Studies were carried out in 69 patients exposed to large-scale surgical operations for various complicated abdominal pathologies in 2007-2014 at the anesthesia and intensive care unit of the Scientific and Surgical Centre named after academician M.A. Topchubashov.

Patients are divided into three groups depending on the type of VNS: I-normotonics-17 patients (24,7%), II-sympathotonics-25 patients (36,2%) and III–vagotonics-27 patients (39,1%). 45 - 60 minutes before the operation patients were administered intramuscular premedications, they were exposed to 500 - 800 ml of pre-infusion and then the epidural cavity was catheterized. The tip of the epidural catheter was placed at the Th_{VI}-Th_{VII} levels in upper abdominal operations, and at Thv_{III}-Th_{X} levels in operations in mid- and lower abdominal sections.

General anaesthesia was started after the injection of the 2 - 3 ml test-dose of 0,5% naropin or marcaine to the epidural cavity. Anaesthesia medications were used in generally accepted doses. 5 - 7 minutes of intubation, total dose (50 - 60 mg) of local anesthetic agent was administered to the epidural cavity in parts by controlling the hemodynamics.

Post-operative pain control was carried out through bolus injection of 20 - 30 mg of naropin or 80 - 120 mg of lidocaine into peridural cavity to be repeated every 6 - 8 hours within 3 - 4 days. If patients continue to complain of pain and discomfort, additionally there were used narcotic and non-narcotic analgesics. The need of patients in narcotic and non-narcotic analgesics in the post-operative period was analyzed based on the VNS type.

Concentration of the adrenocorticotropic hormone (ACTH) and cortisol (Cs) in blood was studied in 3 stages: I – before operation, II – at the most traumatic stage of the operation, III – on I post-operative day. Moreover, hemodynamic indicators such as systolic arterial tension (SAT), diastolic arterial tension (DAT), mean arterial tension (ATmean), heart beat rate (HBR), respiratory minute volume (RMV), myocardial oxygen requirement (MOR), amount of blood sugar and other indicators were studied in 5 stages: I – before operation, II – at the most traumatic stage of the operation, III – 20 minutes after operation, IV – on I postoperative day and V – on II postoperative day.

To determine the VNS type the 1-2 day preoperative electro-encephalography and the following simple functional tests were used:

Cold test: Arterial tension and pulse of a patient are measured in the prone position and recorded. Then the other hand of the patients is put into water at 4°C within 1 minute. Further the pulse and arterial tension were measured every minute until they returned to initial values. Usually it takes 2 - 3 minutes. During the test tension decrease is assessed as vagotony, increase – as sympathotony. When oculocardiac (Aschner-Dagnini) reflex puts pressure on eyeglobe, in normatonics the HBR decreases by 6-12 beats per minute. Heart beat decrease in vagotonics constitutes 12 - 16 beats. On the contrary, in sympathotonics HBR does not change or increases by 2 - 4 beats.

Solar reflex: The examiner puts pressure on the upper abdominal section of a patient lying in prone position until the abdominal aorta pulsation is felt. In normotonics, HBR decreases by up to 4 - 12 beats within 20 - 30 minutes. Other changes are assessed just as in the Aschner-Dagnini reflex.

Ortoclinostatic test: The examination is carried out in two stages. After the measurement of the pulse of a patients in supine position, s/he is offered to immediately get on his/her feet (ortostatic test). In this case, AT increases by up to 20 mm of mercury, and pulse by up to 12 beats. When a patient changes his/her position from vertical to horizontal, AT and pulse values return to initial values within 3 minutes (clinostatictest). Heart acceleration during the clinostatic test demonstrates sympathetic, and decrease – parasympathetic system's activity, prevalence.

Dermographism: Dermographism is vascular reaction of skin against mechanical stimulus. Appearance of a white line in the area of stimulus is assessed as sympathotony – white dermographism, and of a red line - as vagotony – red dermographism. Patients, in which it is impossible to specify the nature of the line were assessed as normotonics.

The nature of viscerovisceral reflex, visserosomatic and viscero-sensor stimulus arising out in the course of anesthesia and operation in the process of determination of the VSN type was considered. For this purpose, the arterial blood tension, pulse, biochemical and metabolic changes occurring in blood were taken as a basis, myocardial oxygen requirement (MOR) was determined by the following formula:

MOR= SAT x HBR /1000 (standard unit)

For the determination of the VNS type in all the patients Vegetative Index Cerdo (VIC) and Hildebrand coefficient (HC) were calculated by the following formula:

VIC = (1 - DAT / HBR) x 1000;

HC = HBR /RMV.

All the figures obtained in the course of investigation were analyzed statistically based on recent recommendations. Group values were lined variationally and a mean indicator (M), standard error of the indicator (m), minimum (min) and maximum (max) values were calculated for each line. At the initial stage of the statistical analysis, the parametric methods were used. Further, given the number of group indicators, to specify the obtained results there were used non-parametric methods. All the calculation was carried out on the EXCELL table.

Results of the study and their discussion

Dynamic changes of the ACTH concentration in all three groups, at three stages are given on the table 1.

Groups	ACTH (7.2 - 63.3 pg/ml)		
	Stage I	Stage II	Stage III
I group (n = 10)	40.9 ± 4.9 (19.07 - 58.5)	139.3 ± 49.5 (70.7 - 584.3)	63.0 ± 1.1^^^ (56.5 - 68.4)
II group (n = 17)	84.3 ± 4.3*** (34.62 - 98.3)	175.2 ± 11.8^^^ (137,2 - 306,8)	75.9 ± 2.2*** (62,2 - 90,6)
III group (n = 15)	76.2 ± 8.0** (14.67 - 103.5)	147.6 ± 9.7^^^ (72.6 - 185.6)	48.1 ± 2.4^^***# # # (23.97 - 60.23)

Table 1: *Comparative Dynamics of ACTH in the blood of the patients of all three groups.*

Note: Statistical accuracy of the difference between indicators:

As compared to stage I: ^^ - $p_1 < 0.01$; ^^^ - $p_0 < 0.01$.

*As compared to group I: ** - $p_1 < 0.01$; *** - $p_1 < 0.001$.*

As compared to group II: # # # - $p_2 < 0.001$.

In the I group patients at the first stage the ACTH constituted 40.9 ± 4.9 pg/ml, that is within normal range, at the II stage, the aggressive stage of operation, it increased up to 139.3 ± 49.5 pg/ml and the III stage decreased up to 63.0 ± 1.1 pg/ml and was at the upper ceiling of the norm. In the II group, that is sympathotonics, ACTH at the I stage constituted 84.3 ± 4.3 pg/ml, and was 2.1 times ($p_1 < 0.001$) higher than in the I group. At the II stage ACTH increased up to 175.2±11.8 pg/ml and was 2.1 times ($p_0 < 0.001$) higher as compared with the I stage and 1.3 times (25.7%) higher as compared with the I group. At the III stage the amount of ACTH in blood decreased up to 75.9 ± 2.2 pg/ml and was 1.1 times (9.9%) lower than at the I stage, and 1.2 times (20.6%) (p1 < 0.01) higher as compared with the I group.

At the I stage in the III group ACTH was 76.2 ± 8.0 pg/ml, that is 1.9 times (86.3%) ($p_1 < 0.01$) higher than in the I group and 1.1 times (9.6%) less than in the II group. At the II stage ACTH increased up to 147.6 ± 9.7 pg/ml, that is 1.9 times (93.8%) ($p_0 < 0.001$) higher than at the I stage, 1.1 times (5.9%) higher than in the I group, 1.2 times (15.7%) lower than in the II group. At the III group the indicator decreased up to 48.1 ± 2.4 pg/ml and was 1.6 times (36.8%) (p0 < 0.01) lower than at the I stage, 1.3 times (23.6%) ($p_1 < 0.001$) as compared with the I group, 1.6 times (36.6%) ($p_2 < 0.001$) as compared with the II group.

Dynamic changes of Cs by stages and groups are shown in the table 2.

Groups	Cortisol (07:00 - 10:00) 171 - 536 ng/ml (16:00 - 22:00) 64 - 327 ng/ml		
	Stage I	Stage II	Stage III
I group (n = 10)	585.0 ± 27.2 (401.4 - 701.0)	1120.6 ± 54.1^^^ (876.8 - 1382.0)	597.6 ± 18.5 (536.0 - 685.0)
II group (n = 17)	771.3 ± 36.7** (452.7 - 964.5	1301.8 ± 64.0^^^ (999.8 - 1837.0)	869.2 ± 38.4*** (538.1 - 998.5)
III group (n = 15)	492.4 ± 17.1**# # # (368.4 - 600.2)	877.0 ± 62.9^^^*# # # (614.2 - 1672.0)	543.2 ± 24.1# # # (498.6 - 870.3)

Table 2: *Compared dynamics of Cs in all the groups of patients at various stages.*

Note: Statistical accuracy of the difference between indicators:

As compared to stage I: ^^^ - $p_0 < 0.01$.

*As compared to group I: * - $p_1 < 0.01$; ** - $p_1 < 0.01$; *** - $p_1 < 0.001$.*

As compared to group II: # # # - $p_2 < 0.001$.

As seen in the table 1, concentration of Cs in the I group was 585.0 ± 27.2 ng/ml at the I stage. At the II state the indicator accurately increased up to ($p_0 < 0.001$), 1120.6 ± 54.1 ng/ml and was 1.9 times (91.6%) higher as compared to the I stage. At the III stage, the amount of Cs in blood decreased up to 597.6 ± 18.5 ng/ml and approached the level of the I stage, that is, the initial value.

In the II group Cs at the I stage was 771.3 ± 36.7 ng/ml, that is 1.3 times (31.8%) (p_1 <0 .01) higher than in the I group. At the II stage dynamic increase of Cs constituted 1301.8 ± 64.0 mmol/l, 1.7 times higher (68.8%) ($p_0 < 0.001$) as compared with the I stage and 1.2 times (16.2%) higher as compared with the I group.

Despite that at the III stage CS dynamically decreased up to 869.2 ± 38.4 mmol/l, it remained 1.1 times (12.7%) higher as compared with the I stage, and 1.5 times (45.4%) ($p_1 < 0.001$) higher as compared with the I group. In the III group, Cs was 492.4 ± 17.1 ng/ml at the I stage, that is 1.2 times (15.8%) ($p_1 < 0.01$) lower than in the I group, and 1.6 times (36.2%) ($p_2 < 0.001$) lower than in the II group.

At the II stage, Cs dynamically increased up to 877.0 ± 62.9 mmol/l, and was 8 times (78.1%) ($p_0 < 0.001$) higher than at the I stage, 1.3 times (21.7%) ($p_1 < 0.05$) higher than in the I group, and 1.5 times (32.6%) ($p_2 < 0.001$) lower than in the II group.

At the III stage, Cs dynamically decreased in the blood plasma up to 543.2 ± 24.1 mmol/l, and despite that it was 1.1 times (10.3%) higher than at the I stage, is was 1.1 times (9.1%) lower than in the I group, and 1.6 (32.6%) ($p_2 < 0.001$) lower than in the II group.

Comparative analysis of neurohormonal changes and changes in other homeostasis indicators in the result of conducted investigation showed that dynamic changes in the level of ACTH and Cs occur in accordance with stages of a surgical operation. Changes observed in hemodynamic indicator are directly proportional with changes in the hormonal status. It means that at a very traumatic stage of a surgical operation, myocardial oxygen requirement (MOR) increase with the increase of SAT, DAT, ATmean indicators. Another noteworthy fact is that already initially, that is at the I stage the level of ACTH and Cs in plasma was statistically accurately higher in sympatotonics, as compared with norma- and vagotonics.

At the II stage, that is, at more traumatic moments of a surgical operation, increase of the level of ACTH in Cs in blood is observed with certain hiper-reaction of the sympatho-adrenal system, which is more expressed in sympatotonics, as compared with normo- and vagotonics. As the changes are short-term, we believe that they are not significant and it is not correct to completely blockage them. Thus, while the sympathetic stress response of an organism to surgical aggression is assessed physiologically, the anaesthetic tactics directed at the deep blockage of the response through anesthesiologic medications may be quite risky. Possible transition of anesthesiologic protection into medicamentous aggression shall be kept in mind during the assessment of the negative effect of the surgical trauma on an organism and selection of anesthesiologic measures against them. Great care shall be taken in this issue and an anesthesiologic tactics requiring differential approach shall be selected.

Results

Results of the study showed, that it is possible to determine the prevalence of the vegetative nervous system through complex assessment of data obtained through the conducted simple tests, EEG, ECG, Vegetative Index Cerdo, Hildebrand Coefficient. Depending on the type of VNS, the comparative analysis of the consumption of CEEA components, that is anesthetics applied in general anesthesia, as well as local anesthetics used for epidural blockage is an anesthesiologically significant and important factor. CEEA has a special place and advantages in the anesthesiological provision of large scale surgical operations on abdominal organs. Epidural blockage - an important component of CEEA, prevents increase of doses of narcotic analgesics and anesthetics for the adequacy of general anesthesia and thus their more express negative effects. At the aggressive stage of a surgical operation (II stage) the amount of stressor hormones in blood statistically significantly increased in all the three groups and then - at the III stage - approached the initial level. In the group, in which sympathomimetic status prevails at the III stage - in sympathomimetics - the level of stressor hormones remain statistically significantly higher than the initial values.

Conclusions

Clinical course of CEEC is characterized by firmer hemodynamic and humoral stability in patients with functional balance of sympathetic and parasympathetic divisions of vegetative nervous system, that is in normotonics in comparison with sympathico and parasympathotonics.

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