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ROLE OF HEART RATE VARIABILITY AND ENDOGENOUS PAIN FACTORS AT VARIOUS SCHEMES OF ANESTHETIC MAINTENANCE OF ABDOMINAL OPERATIONS IN DOGS

The data concerning the use in veterinary medicine of computer analysis of heart rate variability analysis to study the functional state of the autonomic nervous system in dogs at abdominal surgery using traditional and proposed acepromazine-butorphanol-ketamine-propofol anesthesia is presented in the paper. There was found that spectral analysis of heart rate variability allows monitoring of indicators that reflect the functional state of autonomic nervous system activity during anesthesia and surgery. The most informative was the ratio of power spectra of oscillations of low and high frequency LF/HF, reflecting sympathoadrenal-vagal balance. Its level remained stable for acepromazine-butorphanol-ketamine-propofol anesthesia and testified to a sufficient level of analgesia. Levels of cortisol and β-endorphin, which reflect the status of endogenous antinociceptive regulatory mechanisms also testifies the adequacy of anesthesia for acepromazine-butorphanol-ketamine-propofol of anesthesia.

Achievement of adequate pain relief is impossible without taking into account the type of pain reaction. It is known [5] that visceral pain functions also as a independent nosologic unit, differing from somatic pain by insufficient signal value, defective formation of adaptive behavior, inadequate vegetative pain response concerning the needs of the damaged organ and organism as a whole.

Equally important point in evaluating the effectiveness of anesthesia is a state of autonomic nervous system (ANS). Adequacy of compensatory responses of the organism operative trauma and to the neuropharmacologic action and the appropriate course of anesthesia is primarily provided by simulating action of the vegetative nervous system (VNS). Both vegetative disfunction and unbalanced pharmacological action on the VNS can lead to the failure of adaptation in response to surgical trauma with the development of hard-to-control hemodynamic disorders that lead to complications of anesthesia [2]. In this regard, monitoring of VNS state during the pre-, intra-and postoperative periods allows quickly respond to autonomic disorders.

Traditional standards for pre surgical examination does not allow to estimate sufficiently the condition of vegetative homeostasis. The same value of heart rate (HR) and blood pressure (BP) can match different combinations of activity of the sympathetic and parasympathetic ANS parts [6]. At the same time adapted by us analysis of heart rate variability (HRV) allows to estimate the state of ANS in healthy animals.

Purpose of this work is to examine the adequacy of the proposed by us anesthetic intravenous protocol – acepromazine-butorphanol-ketamine-propofol compared with traditional Acepromazine-butorphanol-ketamin and xylazine-butorphanol-thiopental sodium anesthesia at abdominal surgery in dogs by means of spectral analysis of HRV and dynamic of levels of β-endorphin and cortisol.

MATERIAL AND METHODS

Research is carried out on dogs (n=48), from 2 to 10 years old, which were subjected to abdominal operations (with predominance of visceral pain response): coprostasis – 18 heads, splenectomy – 14; bowel resection – 11; hastrotomy – 5. Depending on the mode of anesthesia, animals were divided into three groups, 16 animals in each. For premedication Acepromazine (1%) was injected to dogs of the 1st and 3rd groups in a dose of 0,5 mg/kg. With this purpose to dogs of 2nd group atropine sulfate (0,1%) in doses of 0,03 mg/kg of body weight, and additionaly – Xylazine (2%) in doses of 2 mg/kg was injected subcutaneously. For anesthesia the dogs of 1st group were injected intravenously with Ketamine (5%) at a dose of 8 mg/kg body weight. To the 2nd group of dogs there was applied Thiopental sodium (10%) intravenously in doses of 10 mg/kg body weight. In the 3rd group of dogs there was used mixture containing 7,5 mg Propofol and 12,5 mg Ketamine at a dose of 0,3 ml/kg in 1 ml. If necessary, for lengthening anesthesia the mixture was injected additionally in a dose of 0,15 ml/kg. To enhance analgesic effect previously (20 minutes before anesthesia) Butorphanol tartrate (0,2%) was injected intramuscularly at a dose of 0,6 mg/kg for animals of all groups. To assess the adequacy of anesthesia there was used proved [3] technique for examining the spectral analysis of heart rate variability (SAVSR) in dogs using resuscitative surgical monitor ІОМ-300R. Analysis of heart rate variability (HRV) is a method of assessing the mechanisms of regulation of physiological functions in animals, namely, the total activity of the regulatory mechanisms of neurohumoral regulation of the heart, the relationship between sympathetic and parasympathetic divisions of the autonomic nervous system.

Initial data for spectral analysis of HRV was obtained by electrocardiogram (ECG), which were calculated for 2 min by system aided analysis of heart rhythm. There was assessed the power spec-

tral density in three common ranges: 0,15–0,4 Hz – range of high frequencies (high frequency-HF in ms²) – power in this frequency range reflects vagal activity, 0,04–0,15 Hz – range bass (low frequency – LF in ms²) – in this frequency range electrocardiogram (ECG) activity of the sympathetic nervous system is shown, 0,003–0,04 Hz – very low frequency range (very low frequency – VLF in ms²) – index of activity of humoral regulation and LF/HF – the ratio of power spectra of oscillations of low and high frequencies.

Indicators of HRV were determined in preoperative, intraoperative and postoperative periods. Premedication before and after the operation was carried out general clinical examination and blood samples were taken. The blood plasma was determined by immunoassay method level β-endorphin, using the analyzer «Stat fax» and test system firm Peninsula Laboratories, Inc. (USA), and serum – cortisol levels using test systems company DSL (USA).

RESULTS AND DISCUSSION

Before anesthesia, spectral analysis of HRV indices were in the upper limit of normal, which was installed prior our research [4] or exceeded it. It shows some effort of ANS according to the pathological condition and due to psychoemotional stress in animals. Further at anesthesia there was observed their decline. Thus, the activity level of humoral regulation – VLF, significantly decreased in dogs of all groups (Table). However, if the 1st group, it decreased 1.6 times, then in 2nd – 2,2 times, and in the 3rd – 1,9 times (P<0,05). The similar was dynamics of spectres (HF) and (LF) frequencies. In particular, the level of LF most significantly decreased in group 2 (xylazine-butorphanol-tiopental sodium anesthesia) – 4,2 times (P<0,05), while in 1st – (acepromazine-butorphanol-ketamin anesthesia) – only 1,7 times (P<0,05), and 3rd – on average 2,1 times (P<0,05). Moreover, the activity range of HF frequencies, most significantly decreased also in dogs of the 2nd group – 3,6 times (P<0,05), whereas in dogs the other groups on average – 2,2 times (P<0,05).

Sympathoadrenal-vagal index in animals the first group shifted on 23% (P<0,05) towards predominance of the sympathetic chain ANS, and in the dogs of the 2nd group, on the contrary, it is shifted on 13% (P<0,05) toward parasympathetic activity. In dogs of the 3rd group the reliable changes in sympathoadrenal-vagal balance was not found (P>0,05). It indicates a balanced effect of this combination. Thus, in all schemes of anesthesia inhibition of neurohumoral regulation occurs, but it is the most pronounced for the xylazine-butorphanol-tiopental and acepromazine-butorphanol-ketamin anesthesia with opposite vector inhibitory effect on ANS divisions.

The most traumatic moments of operation are characterized by hesitation of heart rate variability within statistical error. However, it changes in dogs of 2nd group were significantly (P<0,05). Thus, the level of VLF increased 1,2 times (P<0,05), the spectrum of low frequency LF – 3,6 times (P<0,05) and high HF – 2,6 times (P<0,05), which resulted in sympathoadrenal-vagal index, which rose toward the sympathetic ANS level by 41% (P<0,05). This is the evidence of activation of all links ANS, but most significantly of sympathoadrenal, due to nociceptive stimulation and consistent with the results of clinical trials (indexes of heart rate, blood pressure, SpO_2).

After surgery changes of SAVSR were directed towards increasing activity of all parts of the SPA. Thus, in dogs of all groups except the 2nd, parameters of spectral analysis revived at the period before anesthesia. Simultaneously animals of the 2nd group level VLF 1,5 times, and LF and HF – in 1,3 times (P<0,05), remained lower compared to the period prior to anesthesia, reflecting the prolonged recovery period for this scheme of anesthesia.

There were shifting 17% (P<0,05) of sympathetic-vagal balance in sympathoadrenal side in animals of the first group. It is associated with sympathoadrenal effects of ketamine, which may cause undesirable effects such as arrhythmia and increase blood pressure.

Thus, the results were quite informative concerning the control of the course of anesthesia in dogs with abdominal operations and suggest that xylazine-butorphanol-tiopental soium anesthesia in this case is insufficient anesthetic effect on the background of a significant inhibition of the SPA.

Obtained results of research are confirmed by study of such indicators of adequacy anesthesia as β-endorphin and cortisol.

The level of plasma β-endorphin – 0,44±0,01 ng/ml in dog with abdominal pathology did not differ significantly from

Table – **Indices of heart rate variability in dogs at abdominal operations under the different schemes of anesthesia**

Groups of animals, anesthesia protocol	Research period	VLF, ms²	LF, ms²	HF, ms²	LF/HF
First Acepromazine-Butorphanol-Ketamine (n=16)	I	608,4±32,4	495,2±21,2	546,7±28,1	0,9±0,04
	II	384,8±25,6*	269,8±17,4*	242,4±19,3*	1,11±0,04*
	III	397,5±26,2*	285,6±18,1*	267,7±20,1*	1,06±0,03*
	IV	559,7±29,8°	461,7±23,6°	439,8±23,4*°	1,05±0,04*
Second Xylazine-Butorphanol-Thiopental (n=16)	I	549,6±30,2	501,2±33,4	564,3±29,2	0,89±0,03
	II	254,2±16,4*	120,4±13,5*	155,2±16,0*	0,77±0,02*
	III	311,5±19,7*°	437,1±28,2°	401,3±23,7*°	1,09±0,04*°
	IV	371,3±22,5*	381,7±25,3*	441,4±23,1*	0,86±0,03°
Third Acepromazine-Butorphanol-Ketamine-Propofol (n=16)	I	531,4±26,4	429,3±16,1	397,4±17,4	1,08±0,03
	II	302,3±20,5*	200,6±14,2*	196,6±14,3*	1,02±0,04
	III	324,7±23,7*	213,9±15,3*	204,9±14,9*	1,04±0,04
	IV	507,8±28,2°	389,1±18,7°	380,7±19,1°	1,02±0,03

Notes. 1. I – before anesthesia, II – during anesthesia, III – the most traumatic moments, IV – after surgery.
2. P – *P<0,05, remaining P>0,05, compared to anesthesia, °P<0,05; remaining P>0,05, compared with the previous data in the group.

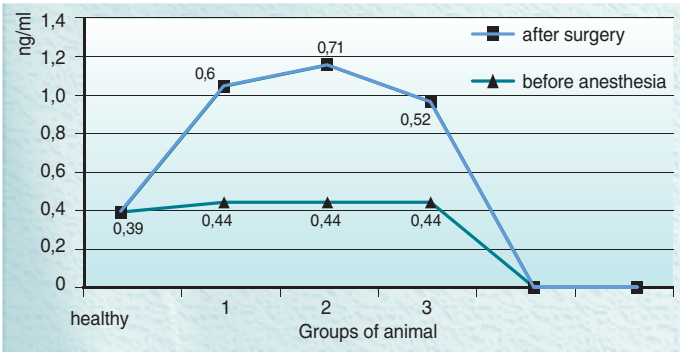

Fig. 1. The level of β-endorphin in the blood of dogs with abdominal operations under different schemes of anesthesia

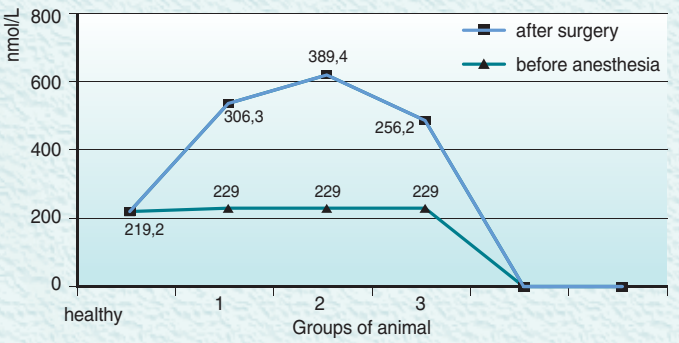

Fig. 2. Levels of cortisol in the blood of dogs during abdominal operations under different schemes of anesthesia

healthy – 0,39±0,03 ng/ml (Fig. 1). After surgery, it increased in all groups of dogs, indicating activation of the antinociceptive system. However, if in animals of the 3rd group content in blood β-endorphin increased only 1,2 times (P<0,05) and amounted to 0,52±0,02 ng/ml, in the dogs in group 2 – 1,6 times (P<0,05) to – 0,71±0,03 ng/ml, that was the biggest compared to other groups (P<0,05). In dogs of the 1st group β-endorphin level was within 0,58–0,62 ng/ml. It indicates that the use of xylazine-butorphanol-tiopental anesthesia does not provide sufficient analgetic protection, which leads to activation of endogenous antinociceptive systems.

In general, the results of research of the level of β-endorphin in plasma of operated dogs indicate activation of antinociceptive systems even in groups of animals, where analgesia was adequate, that is probably due to presence of ketamine anesthesia circuits, which are known [1] on unlike other general anesthetics activate antinociceptive structures even before nociceptive stimuli.

Before anesthesia the level in the blood of dogs of stress hormone cortisol was 229,0±4,7 nmol/l and also had no probable difference (P>0,05) from clinically healthy animals – 219,2±6,9 nmol/l (Fig. 2), indicating that small stress-provoking effect of noxious load specified for abdominal pathology.

After surgery there were found increased levels of cortisol in the blood of dogs of all groups. The highest it was in the 2nd group – 389,4±8,6 nmol/l, that 70% higher than its preoperative level (P<0,001). This reaction shows a significant strain of its adaptation mechanisms, that in the event of additional factors (significant nociceptive stimulation, blood loss, hypoxemia) can lead to the development of critical states (shock, cardiac arrest, breathing).

At the same time there was a minimum increase of cortisol levels in dogs of the 3rd group – 12% (P<0,05), indicating on the one side the adequate anesthetical protection, on the other – the stress-limitative effect of Acepromazine-butorphanol-ketamine-propofol anesthesia. In animals of the second group cortisol levels increased after surgery in 34% (P<0,001), which also shows the stress adaptive mechanisms in response to anesthesia and operating components of trauma, but to a lesser extent – on average in a half than in second group of dogs.

Thus, blood levels of β-endorphin and cortisol indicate adequate anesthetical protection only by acepromazine-butorphanol-ketamine-propofol circuit anesthesia. Instead, xylazine-butorphanol-tiopental anesthesia does not provide adequate antinociceptive protection and requires additional use of analgesics for abdominal operations mostly by visceral type of pain reaction.

The course of anesthesia includes extremely important moment of recovery of functions of the central nervous system and the whole body of animals in the postoperative period. It turned out that the recovery period after anesthesia was the shortest in dogs of the 3rd group, which were used – 17,3±2,4 min. Instead, the most of its period was recorded in the 2nd group, where it lasted 3,3 times longer than in the 3rd (P<0,05). In this regard, itshould be noted that one of the main requirements for adequacy of anesthesia is its control. Until recently, it succeeded only at the application of inhaled anesthetics. However, the results of our study of using short effect anesthetics (ketamine) and ultrashort (propofol) action makes it possible to achieve adequate control of anesthesia at their compatible intravenous administration.

CONCLUSIONS

1. Spectral analysis of HRV during preparation and in the process of anesthetic surgery makes it possible to assess objectively the state of autonomic regulation and react at significant risk of complications in the intra-and postoperative periods.

2. Concerning the clinical characteristics of anesthesia, the results of spectral analysis of HRV (lack of reliable changes in sympathoadrenal-vagal balance (P> 0,05)), and changes in levels of β-endorphin, cortisol application acepromazine-butorphanol-ketamine-propofol anesthesia in dogs by abdominal operations makes it possible to achieve adequate anesthesia, analgesia and rapid recovery from anesthesia.

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Роль варіабельності серцевого ритму та ендогенних знеболювальних факторів за різних схем анестезіологічного забезпечення абдомінальних операцій у собак. *С.В. Рубленко, М.В. Рубленко, В.М. Власенко, В.Г. Андрієць*

Наведено дані щодо застосування у ветеринарній медицині комп'ютерного аналізу варіабельності ритму серця для дослідження функціонального стану вегетативної нервової системи в собак за абдомінальних оперативних втручань із використанням традиційних та запропонованої ацепромазин-буторфанол-кетамін-пропофолової анестезії. Встановлено, що спектральний аналіз варіабельності серцевого ритму дає можливість проводити моніторинг показників, які відображають функціональний стан активності автономної нервової системи під час анестезії та оперативного втручання. Найбільш інформативним виявився показник співвідношення потужності коливань спектрів низької та високої частот LF/HF, що відображає симпато-вагусний баланс. Його рівень за ацепромазин-буторфанол-кетамін-пропофолової анестезії залишався стабільним і свідчив про достатній рівень аналгезії. Рівні кортизолу та β-ендорфіну, які відображають стан ендогенних антиноцицептивних регуляторних механізмів, також свідчили про адекватність знеболювання за такої анестезії.

Роль вариабельности сердечного ритма и эндогенных обезболивающих факторов при различных схемах анестезиологического обеспечения абдоминальных операций у собак. *С.В. Рубленко, М.В. Рубленко, В.М. Власенко, В.Г. Андриец*

Приведены данные о применении в ветеринарной медицине компьютерного анализа вариабельности ритма сердца для исследования функционального состояния вегетативной нервной системы у собак при абдоминальных оперативных вмешательствах с использованием традиционных и предложенной ацепромазин-буторфанол-кетамин-пропофоловой анестезии. Установлено, что спектральный анализ вариабельности сердечного ритма позволяет проводить мониторинг показателей, отражающих функциональное состояние активности автономной нервной системы во время анестезии и оперативного вмешательства. Наиболее информативным оказался показатель соотношения мощности колебаний спектров низкой и высокой частот LF/HF, отражающий симпато-вагусный баланс. Его уровень при ацепромазин-буторфанол-кетамин-пропофоловой анестезии оставался стабильным и свидетельствовал о достаточном уровне аналгезии. Уровни кортизола и β-эндорфина, отражающие состояние эндогенных антиноцицептивных регуляторных механизмов, также свидетельствовали об адекватности обезболивания при такой анестезии. ○