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Research Article

Optimization of premedication of patients with arterial hypertension and severe ventricular rhythm disturbances with Amiodarone-associated thyrotoxicosis

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Abstract

Introduction: The effectiveness of premedication of patients with arterial hypertension and severe ventricular rhythm disturbances against the background of Amiodarone-associated thyrotoxicosis, high anxiety and cyclothymiae disorders should be based on the pharmacological positions of the need to reduce the risk of dangerous adverse cardiovascular reactions.

Materials and methods: During the research, a clinical group of 114 patients with arterial hypertension, severe ventricular arrhythmias and Amiodarone-associated type I thyrotoxicosis was formed: four subgroups were identified. In Subgroup 1 (n=22), no premedication was given. In Subgroup 2 (n=32), premedication was given with Diazepam and magnesium sulfate in a prolonged mode. In Subgroup 3 (n=30), the patients received Diazepam the day before surgery. In Subgroup 4 (n=30), premedication was given with Midazolam. A dynamic assessment of the severity of anxiety, depression, sedation and daily monitoring of blood pressure and ECG were carried out.

Results and discussion: After surgery, in Subgroup 1, the level of anxiety and depression increased. In all other Subgroups, regardless of the type of premedication, the use of benzodiazepines was accompanied by a decrease in the level of anxiety after surgery. A decrease in pressure load and an increase in the stability of the parameters of systemic hemodynamics were registered in Subgroup 2 of patients, whereas in Subgroup 4 of patients, the pressure load increased while limiting the differences in blood pressure values during the day. After surgery, in Subgroup 2, cardiac rhythm disturbances were less common; in Subgroup 3, the structure of rhythmogenesis disturbances in the heart almost did not change, and in Subgroup 4, there was an unfavorable trend of an increase in the frequency of supraventricular, single and group ventricular extrasystoles.

Conclusion: The prolonged premedication with long-acting benzodiazepines and magnesium preparations in patients with arterial hypertension, ventricular rhythm disturbances against the background of Amiodarone-associated thyrotoxicosis reduces the level of anxiety, as well as the risk of developing cardiovascular complications and instability of systemic hemodynamics.

Keywords

Amiodarone, arrhythmia, arterial hypertension, benzodiazepines, thyrotoxicosis, side effects, premedication.

Introduction

For neurosurgery on the spinal cord and brain in patients with arterial hypertension (AH) with cardiac rhythm disturbances taking Amiodarone for a long time, pre-surgical preparation should be carried out taking into account the presence or absence of thyroid dysfunction. At the same time, thyroid gland diseases can be detected at the stage of preparing a patient for surgery. When urgent surgery is indicated, Amiodarone cannot be discontinued even with a change in the thyroid status due to the need to prevent ventricular fibrillation in fatal ventricular rhythm disturbances (Bogazzi et al. 2010; Laina et al. 2016). In such a difficult clinical situation, a high level of anxiety and cyclothymia disorders in connection with the upcoming neurosurgery, lability of the patient's psyche, variability of systemic hemodynamics, cardiac effects of excess thyroid hormones against the background of the use of Amiodarone are of serious danger (Negovsky et al. 2008; Claro et al. 2015; Vorobiev and Mitrokhin 2018). Special control over the correction of fatal severe cardiac rhythm disturbances in high-risk hypertension is needed, in combination with Amiodarone-associated thyrotoxicosis with simultaneous elimination of adverse mental and cardiovascular reactions. The solution to this clinical issue is seen in the competent pharmacological premedication practices (Jawaid et al. 2007; Jafar and Khan 2009; Kitiashvili et al. 2018).

The use of long-acting benzodiazepines along with magnesium preparations at the premedication stage can provide hypnotic, sedative, anxiolytic, central and peripheral muscle relaxant effects along with increased hemodynamic stability in the post-surgery period (Donen 2002; Ebirim and Tobin 2010; Ivankova and Eroshevich 2010; Fisher et al. 2017; Lahkar and Dutta 2019; Zhusupova et al. 2019). The antiarrhythmic, hypotensive, sedative, vasodilating effects of magnesium sulfate supplements, enhances the effects of long-acting benzodiazepines, and provides a rational combination of drugs at the stage of premedication of patients (Zhoniev and Rakhimov 2014). Besides, parenteral administration of magnesium sulfate promotes dilatation of coronary arteries against the background of a decrease in total peripheral resistance, which is important in hypertension with left ventricular hypertrophy. Meanwhile, when preparing patients for surgery, short-acting benzodiazepines are more often used, providing deeper and faster sedation (Zhoniev and Rakhimov 2014; Badikova and Zhenilo 2017). The combination of long-acting benzodiazepines with parenteral administration of magnesium sulfate in a prolonged mode before surgery in hypertensive patients with severe cardiac rhythm disturbances against the background of Amiodarone-associated thyrotoxicosis is a new solution requiring a study of the clinical efficacy of this approach.

The effectiveness of pre-surgical preparation of high-risk hypertensive patients with fatal severe cardiac rhythm disturbances, against the background of Amiodarone-associated thyrotoxicosis, should be based not only on the principles of anesthesiology and resuscitation, but also on the pharmacological positions of the need to correct anxiety and cyclothymia disorders and to reduce the risk of dangerous side effects of cardiovascular reactions in the post-surgery period (Loh 2000; Martino et al. 2001; Tanda et al. 2008; Raghavan et al. 2012; Ortiz et al. 2017).

The aim of the study was to develop a rational combination of drugs and a premedication regimen in patients with arterial hypertension and severe cardiac rhythm disturbances against the background of Amiodarone-associated thyrotoxicosis when preparing them for neurosurgery.

Materials and methods

The dissertation was approved by the local independent ethical committee of the Federal State Budgetary Educational Institution of Higher Education "Rostov State Medical University" of Ministry of Health of the Russian Federation (Minutes No. 18/17 dated 26.10.2017). All the patients signed an informed consent to participate in the study.

General characteristics of the groups

During the study, a clinical group of 114 patients with arterial hypertension, severe cardiac rhythm disturbance and Amiodarone-associated type I thyrotoxicosis was formed. Type I thyrotoxicosis was detected at the stage of preparing the patients for surgery.

The criteria for including the patients in the clinical group were as follows: high risk stages 2–3 type I arterial hypertension, lasting for 10 years or more; left ventricular hypertrophy with a posterior wall thickness of more than 14 mm; combined antihypertensive therapy with angiotensin II receptor antagonists (Losartan at a daily dose of 50–100 mg) and a non-thiazide diuretic (Indapamide at a daily dose of 1.25–2.5 mg); fatal ventricular arrhythmias; taking Amiodarone to treat ventricular arrhythmias resistant to antiarrhythmic drugs of other groups; subclinical Amiodarone-associated mild type I thyrotoxicosis (decrease in the level of thyroid-stimulating hormone less than 0.1 mIU/L along with the normal level of free thyroxine and triiodothyronine in a subclinical course); preparation for neurosurgery (discectomy, decompression and stabilization of regions of spine in degenerative-dystrophic diseases, spinal injuries), which does not imply long-term planned preparation. The distribution of patients depending on the nature of neurosurgery was random.

The criteria for excluding the patients from the main and clinical groups are as follows: ischemic heart disease, unstable angina; dilated cardiomyopathy, hemodynamically significant heart defects, chronic heart failure; stroke or myocardial infarction within 6 months before inclusion in the research; Amiodarone-associated type II thyrotoxicosis; decompensation of renal or hepatic failure.

Patients received Amiodarone at a daily dose of 200 mg. The duration of Amiodarone intake was on average 6.4±0.4 years. After diagnosing thyrotoxicosis, due

to a high risk of ventricular fibrillation in severe cardiac rhythm disturbances, the patients received the standard thyrostatic therapy – Thiamazole at an average concentration of 10 mg/day.

The patients, depending on the premedication availability and scheme, were divided into four subgroups: in Subgroup 1 (n=22), premedication was not given; in Subgroup 2 (n=32), premedication was given with Diazepam (three days before surgery, 5–10 mg orally at night, and 1 hour before anesthesia, 0.5% solution at a dose of 0.15 mg/kg i.m.). Before surgery, 5 ml of 25% solution of magnesium sulfate was additionally injected; in Subgroup 3 (n=30), the patients received Diazepam orally at night (5–10 mg) and 1 hour before anesthesia at a dose of 0.15 mg/kg i.m.; in Subgroup 4 (n=30), premedication was given with Midazolam, 0.5% solution at a dose of 0.07–0.1 mg/kg i.m., 40–60 minutes before anesthesia.

In Subgroup 1, the average age was 59.9±1.93 years (median – 61 years), in Subgroup 2 – 57.9±1.72 years (median – 61 years), in Subgroup 3 – 60.9±2.04 (median – 62 years) and in Subgroup 4 – 59.8±2.56 years (median – 60 years). The ratio of the number of men and women in Subgroup 1 was 14 (64%) and 8 (36%), in Subgroup 2 – 22 (69%) and 10 (31%), in Subgroup 3 – 18 (60%) and 12 (40%), in Subgroup 4 – 20 (67%) and 10 (33%), respectively.

Combined antihypertensive therapy was not discontinued before and after surgery. During the surgery, anesthesia was unified for all the patients: Propofol 6–7 mg/kg/hour and Phentanyl 0.1 mg/10 kg/hour in the first hour of surgery, 0.05 mg/10 kg/hour in the second hour and 0.03 mg/10 kg/hour in the third and subsequent hours.

All the patients underwent neurosurgery in connection with post-traumatic conditions and degenerative-dystrophic diseases, which did not imply delays in surgery and long-term somatic and endocrinological preparation of patients for it.

Evaluation of the effectiveness of various premedication methods

Ramsay sedation score in the post-surgery period in the intensive care unit was carried out hourly until the condition was stabilized.

When assessing the depth of sedation using an A-2000XP monitor (Aspect Medical Systems, USA), an EEG signal was recorded, after which the bispectral index (BIS) was calculated. This indicator made it possible to determine a degree of inhibition of brain function or the depth of sedation in real time.

To study the level of anxiety and depression, the Hospital Anxiety and Depression Scale (HADS) was used.

For 24-hour blood pressure monitoring, an oscillometric method and a BPlab device (Petr Telegin, Nizhny Novgorod) were used from 7 am to 11 pm, blood pressure was recorded sequentially every 15 minutes, and from 11 pm to 7 am – every 30 minutes.

The daily ECG monitoring was carried out using an eight-channel cardiac monitor “Kardiotekhnika04” (JSC Inkart, St. Petersburg). In the analysis of ventricular extrasystoles, the classification according to B. Lown (according to the severity scale) was used.

Daily monitoring of blood pressure and ECG, assessment of anxiety in three subgroups made it possible to assess the effectiveness of various methods of premedication for reducing the risk of dangerous cardiovascular reactions in the post-surgery stage.

Statistical analysis

The statistical processing of the research results was carried out using the STATISTICA 12.0 software (StatSoft, USA). The $\chi 2$ test was used to analyze and compare the qualitative indicators, and the Kruskal-Wallis and Mann-Whitney analysis-of-variance tests were used for the quantitative ones. The distribution normality was checked using the Shapiro-Wilk test. The level of statistical significance of the difference between the indicators was taken at $p<0.05$.

Results and discussion

The optimization of the premedication phase is an urgent issue of medicine and clinical pharmacology, because it is aimed at preventing adverse and unpredictable changes in the functional status of the patient at the surgery stage and in the early post-surgery period (Caumo et al. 2001; Marfin 2017). The optimization of premedication of patients with neurosurgical pathology, taking into account the hemodynamic and vegetative status, the level of neurovegetative control of systemic hemodynamics and rhythmogenesis in the heart with long-term elevated blood pressure, will improve treatment results and reduce the length of stay of neurosurgical patients in the intensive care units and in-patient facilities. The degree of research to study the effectiveness of prolonged premedication of patients with arterial hypertension, fatal cardiac rhythm disturbances and Amiodarone-associated thyrotoxicosis for the correction of high anxiety and cyclothymia disorders and reduction of cardiovascular complications in the post-surgery period is low. In the literature, there are single publications on the features of premedication of patients with thyrotoxicosis when performing thyroid gland surgery (Badikova et al. 2020). At the same time, the aspects of premedication are studied in the planned preparation of a patient for surgery after reaching euthyroidism.

The level of anxiety and depression in patients before and after surgery was analyzed according to the HADS scale (Table 1). Before surgery, the level of anxiety and depression in the patients of the four subgroups had the rank of clinically expressed anxiety and depressive syndrome, which determined the necessity for using premedication.

After surgery, in Subgroup 1, the level of anxiety increased from 11.5±0.57 to 14.7±0.89 points (p=0.039), and depression – from 7.8±0.4 to 9.4±0.7 points (p=0.045). In all other subgroups, regardless of the type of premed-

Table 1. Level of Anxiety and Depression, Bispectral Index in Subgroups of Patients Depending on the Tactics of Premedication Before and After Surgery

Indicators	Period	Subgroup 1 (n=22)	Subgroup 2 (n=32)	Subgroup 3 (n=30)	Subgroup 4 (n=30)	p_{all}
Anxiety level, points	Before	11.5±0.57	11.2±0.64	11.3±0.61	11.4±0.75	0.97
	After	14.7±0.89	8.6±0.57	8.9±0.58	9.3±0.73	0.88
	$p_{before-after}$	**0.039**	**0.041**	**0.040**	**0.047**	
Depression level, points	Before	7.8±0.4	7.4±0.5	7.9±0.4	7.7±0.3	0.92
	Afte	9.4±0.7	6.7±0.7	7.0±0.6	6.8±0.8	0.90
	$p_{before-after}$	**0.045**	0.74	0.63	0.81	
BIS, %	After surgery	94.5±0.5	94.2±0.4	93.9±0.8	94.1±0.6	0.98

Note: Subgroup 1 – no premedication, Subgroup 2 – prolonged premedication with Diazepam, Subgroup 3 – premedication with Diazepam one day before surgery, Subgroup 4 – premedication with Midazolam before anesthesia. BIS – bispectral index. $p_{before-after}$ – confidence probability of the difference between the indicators before and after the surgery, p_{all} – confidence probability of the results of the analysis of variance comparing the indicators of the four subgroups.

ication, the use of benzodiazepines was accompanied by a decrease in the level of anxiety after surgery (Table 1). The depression level after surgery, the bispectral index, the recovery of brain activity 12 hours after surgery did not differ in the clinical subgroups (Table 1).

The adequacy of the sedation level after surgery was assessed using the Ramsay scale (Table 2).

One hour after surgery, the sedation level in the patients of all three subgroups was 6, which corresponded to the state when the patient was asleep and did not respond to stimuli. Three-six hours after surgery, sedation levels of 2 and 3 points prevailed in all three subgroups. After 12 hours, sedation levels were similar at 1–2 point(s). Thus, sedation was similar in the four subgroups after surgery.

Table 2. Distribution of Patients Depending on the Level of Sedation According to the Ramsay Scale in the Post-surgery Period in Patients' Subgroups, Depending on the Tactics of Premedication

Group	Observation period	Sedation level	Number	
			Abs.	%
Subgroup 1 (n=22)	1 hour after surgery	6	22	100.0
	3–6 hours after surgery	2	5	22.7
		3	14	63.6
		4	2	9.1
	12 hours after surgery	2	13	59.1
		1	9	40.9
Subgroup 2 (n=32)	1 hour after surgery	6	16	100.0
	3–6 hours after surgery	2	5	31.25
		3	9	56.25
		4	2	12.5
	12 hours after surgery	2	5	31.25
		1	11	68.75
Subgroup 3 (n=30)	1 hour after surgery	6	15	100.0
	3–6 hours after surgery	2	6	40.0
		3	7	46.7
		4	2	13.3
	12 hours after surgery	2	7	46.7
		1	8	53.3
Subgroup 4 (n=30)	1 hour after surgery	6	15	100.0
	3–6 hours after surgery	2	7	46.7
		3	7	46.7
		4	1	6.7
	12 hours after surgery	1	15	100.0
p_{all}	1 hour after surgery		6 points p_{all} = 1.0	
	3–6 hours after surgery		2 points p_{all} = 0.68	
			3 points p_{all} = 0.83	
			4 points p_{all} = 0.81	
	12 hours after surgery		2 points p_{all} = 0.39	
			1 points p_{all} = 0.01	

Note: Subgroup 1 – no premedication, Subgroup 2 – prolonged premedication with Diazepam, Subgroup 3 – premedication with Diazepam one day before surgery, Subgroup 4 – premedication with Midazolam before anesthesia. p_{all} – confidence probability of the difference between the indicators of the four subgroups.

Table 3. Dynamics of Average Daily, Daytime and Nighttime Parameters of Daily Monitoring of Blood Pressure (M±m) in Subgroups of Patients After Surgery (on the Third Day), Depending on the Tactics of Premedication Against the Background of Stable Antihypertensive Therapy (Angiotensin II Receptor Antagonist+Non-thiazide Diuretic)

Indicators / Subgroups		Subgroup 1 (n=22)	Subgroup 2 (n=32)	Subgroup 3 (n=30)	Subgroup 4 (n=30)	p_{all}
SAP24, mm Hg	before	141.2±2.4	137.2±3.1	135.6±2.6	134.8±2.9	0.48
	after	153.6±2.8	130.5±2.4′	140.4±3.1′*	142.7±3.3′*	**0.025**
$p_{before-after}$		**0.031**	**0.042**	0.087	**0.039**	
DAP24, mm Hg	before	84.7±2.0	82.1±2.3	81.4±2.5	83.0±1.8	0.35
	after	85.6±2.1	81.9±2.0	82.6±1.9	85.7±2.4	0.51
$p_{before-after}$		0.49	0.84	0.72	0.58	
HR24, bpm	before	83.1±1.5	80.4±1.6	81.5±1.3	82.7±1.9	0.88
	after	89.4±2.3	73.5±1.8′	80.9±2.2′*	84.9±2.1*°	**0.035**
$p_{before-after}$		**0.048**	**0.027**	0.71	0.46	
SAP at daytime, mm Hg	before	145.3±3.1	139.5±3.2	141.6±4.0	138.1±2.7	0.27
	after	155.3±5.2	133.7±2.8′	144.1±3.7′*	145.8±3.1′*	**0.033**
$p_{before-after}$		**0.039**	**0.05**	0.26	**0.046**	
DAP at daytime, mm Hg	before	88.2±2.7	86.5±2.8	84.9±3.3	87.5±2.9	0.75
	after	95.3±3.1	82.4±2.4′	85.5±2.6′	93.3±2.5*°	**0.048**
$p_{before-after}$		**0.028**	0.58	0.76	**0.049**	
HR at daytime, bpm	before	86.4±2.1	83.6±1.8	84.3±1.7	85.1±1 .5	0.94
	after	90.2±2.9	76.1±2.0′	84.8±2.1′*	88.5±2.3*°	**0.042**
$p_{before-after}$		0.13	**0.036**	0.99	0.92	
SAP at nighttime, mm Hg	before	133.7±2.9	128.6±2.7	132.5±3.1	130.4±3.4	0.56
	after	140.2±4.9	127.1±2.5′	138.9±2.8*	140.2±3.1*	**0.031**
$p_{before-after}$		**0.027**	0.87	**0.049**	**0.021**	
DAP at nighttime, mm Hg	before	81.8±1.9	80.1±2.6	79.2±2.9	82.4±2.5	0.91
	after	81.3±3.7	78.4±2.2	80.1±3.1	84.8±2.3	0.58
$p_{before-after}$		0.94	0.94	0.92	0.85	
HR at nighttime, bpm	before	66.0±1.3	62.6±1.5	64.7±1.3	68.4±1.4	**0.044**
	after	75.2±1.9	64.2±1.4′	65.8±1.2′	67.9±1.6′	0.87
$p_{before-after}$		0.14	0.53	0.64	0.72	

Note: $p_{before-after}$ – confidence probability of the difference between the indicators before and after the surgery, p_{all} – confidence probability of results of the analysis of variance comparing the indicators of the four groups,′ – statistically significant difference in pairwise comparison, compared with Subgroup 1, * – compared with Subgroup 1, ° – compared with Subgroup 2 at $p<0.05$, p/s – post-surgery. Subgroup 1 – no premedication, Subgroup 2 – prolonged premedication with Diazepam, Subgroup 3 – premedication with Diazepam one day before surgery, Subgroup 4 – premedication with Midazolam before anesthesia. SAP – systolic arterial pressure, DAP – diastolic arterial pressure, SAP24 – average daily systolic arterial pressure, DAP 24 – average daily diastolic arterial pressure.

Initially before surgery, the systemic hemodynamic parameters were adjusted with antihypertensive drugs in the four patients' subgroups. There were no statistically significant differences between the groups (Table 3).

In the patients of Subgroup 1, in the absence of premedication after surgery, there was an increase ($p<0.05$) in average daily, daytime and nighttime systolic arterial pressure, daytime DAP and HR during the day. Benzodiazepines used in premedication are combined with angiotensin II receptor antagonists and a non-thiazide diuretic, which made it possible not to cancel antihypertensive therapy in the patients of the studied subgroups before and after surgery. In Subgroup 2 of patients, in the first three days after surgery, the mean daily systolic arterial pressure was lower compared to Subgroup 3 ($p = 0.025$) (130.5±2.4 versus 140.4±3.1 mm Hg) and Subgroup 4 (130.5±2.4 mm Hg vs 142.7±3.3 mm Hg) in the absence of intergroup differences in diastolic arterial pressure between groups ($p=0.51$) (Table 3).

Thus, a decrease in pressure load and an increase in the stability of the parameters of systemic hemodynamics were registered in Subgroup 2 of patients with combined and prolonged premedication (Diazepam and magnesium sulfate), and in Subgroup 3 of patients (Diazepam given as a single doze), the pressure load increased when the differences in blood pressure values per day were limited. In Subgroup 4, with a single use of a short-acting benzodiazepine, there was an increase ($p<0.05$) in the average daily, daytime and nighttime systolic arterial pressure, and DAP in the daytime during the first three days after surgery.

With 24-hour ECG monitoring in the patients of Subgroup 1 without premedication, the dynamics of the frequency and quantitative characteristics of supraventricular and ventricular extrasystoles after surgery was unfavorable. In Subgroup 2, in the post-surgery period, the frequency of supraventricular extrasystoles was the lowest (37.5%), whereas it was more common in Sub-

Table 4. Dynamics of the Quantitative Characteristics of Extrasystoles During the Day According to the Results of ECG Monitoring in Subgroups of Patients After Surgery (on the Third Day) Depending on the Tactics of Premedication

Indicators	Subgroups	Subgroup 1 (n=22)	Subgroup 2 (n=32)	Subgroup 3 (n=30)	Subgroup 4 (n=30)	p_{all}
Number of supra-ventricular extrasystoles per day	Before	573.2±13.4	478.3±11.2	501.9±12.8	556.7±11.7	0.37
	After	712.5±12.8	213.7±10.4′	457.6±11.9′*	642.5±10.3′*°	**0.01**
$p_{before-after}$		**0.003**	**0.001**	0.08	**0.031**	
Number of single ventricular extrasystoles	Before	211.5±14.7	189.2±9.5	195.3±8.5	201.5±9.0	0.85
	After	324.1±21.6	123.6±8.2′	178.4±9.1′*	318.6±14.6*°	**0.02**
$p_{before-after}$		**0.017**	**0.024**	0.24	**0.027**	
Number of group ventricular extrasystoles	Before	21.4±1.4	18.9±2.3	19.6±1.5	21.3±1.8	0.28
	After	31.2±1.9	11.3±1.4′	16.5±1.0′*	25.7±1.1*°	**0.01**
$p_{before-after}$		**0.008**	**0.013**	**0.045**	0.26	

Note: $p_{before-after}$ – confidence probability of the difference between the indicators before and after the surgery, p_{all} – confidence probability of results of the analysis of variance comparing the indicators of the four groups,′ – statistically significant difference in pairwise comparison, compared with Subgroup 1, * – compared with Subgroup 1, ° – compared with Subgroup 2 at $p<0.05$, p/s – post-surgery. Subgroup 1 – prolonged premedication with Diazepam, Subgroup 2 – premedication with Diazepam one day before surgery, Subgroup 3 – premedication with Midazolam before anesthesia.

group 3 (60%) and Subgroup 4 (80%). The frequency of single ventricular extrasystoles was observed in fewer patients in Subgroup 2 (37.5%) compared to Subgroup 3 (46.7%) and Subgroup 4 (60%). The frequency of group ventricular extrasystoles, runs of ventricular tachycardia in the subgroups of patients receiving premedication after surgery was low and did not differ, and in the absence of premedication it was observed in 4 patients (18%).

Whereas the frequency characteristics of extrasystoles during the day according to the results of ECG monitoring in subgroups of patients after surgery did not change, the quantitative characteristics were dynamically rearranged in different directions depending on the tactics of premedication (Table 4).

In Subgroups 1 and 4, the numbers of supraventricular extrasystoles and single ventricular extrasystoles during the day after surgery increased compared to the pre-surgical period. In Subgroup 1 after surgery, runs of life-threatening group ventricular extrasystoles were more common. In Subgroup 2, after surgery, the numbers of supraventricular extrasystoles per day (213.7±0.4), single ventricular extrasystoles (123.6±8.2) and group ventricular extrasystoles (11.3±1.4) were the smallest, and in Subgroup 4, the largest values were the number of supraventricular extrasystoles per day 642.5±10.3, the number of single ventricular extrasystoles 318.6±14.6 and the number of group ventricular extrasystoles 30.7±1.1. After surgery, compared with the initial pre-surgical level in Subgroup 2, the numbers of supraventricular extrasystoles, single and group ventricular extrasystoles decreased, respectively, by 266.1±11.6 (p=0.001), 64.2±3.5 (p=0.024) and 7.5±0.4 (p=0.013). In Subgroup 3, only the number of group ventricular extrasystoles significantly decreased (p=0.045). In Subgroup 4, the numbers of supraventricular extrasystoles, single and group ventricular extrasystoles increased, respectively, by 184.5±9.5 (p=0.031), 117.5±2.9 (p=0.027) and 9.3±0.7 (p=0.048).

Thus, after surgery, cardiac rhythm disturbances in Subgroup 2 were less common; in Group 3, the structure of rhythmogenesis disturbances in the heart almost did not change, and in Subgroup 4, there was an unfavorable trend towards an increase in the frequency of supraventricular, single and group ventricular extrasystoles.

Therefore, the use of complex prolonged premedication with long-acting benzodiazepines and magnesium preparations prevents the development of serious undesirable side reactions of the drug therapy for thyrotoxic syndrome and worsening of symptoms of the cardiovascular system.

Thus, the individual tactics of pre-anesthetic preparation of patients with arterial hypertension and fatal ventricular rhythm disturbances taking Amiodarone for a long time helps to reduce the risk of anxiety and dangerous adverse cardiovascular reactions in the early post-surgery period. The long-term administration of Amiodarone for more than five years at a dose of 200 mg per day made it possible to achieve an antiarrhythmic effect. Despite the diagnosed subclinical Amiodarone-associated mild thyrotoxicosis, the need to continue therapy with Amiodarone was associated with the absence of the effect of antiarrhythmic drugs of other groups (of classes I, II and IV), the presence of left ventricular hypertrophy with a posterior wall thickness of more than 14 mm (a contraindication for the use of Sotalol as a class III antiarrhythmic drug). The prolonged premedication with long-acting benzodiazepines and magnesium preparations was accompanied by a favorable effect simultaneously to anxious-depressive symptoms and the cardiovascular system within the first three days after the surgery: there was a decrease in the frequency of disturbances of rhythmogenesis in the heart, the frequency of heart contractions, systolic arterial pressure against the background of a decrease in the level of anxiety. The use of short-acting benzadiazepines in premedication was not accompanied by an increase in anxiety and depression in the early post-surgery period, but did not prevent adverse cardiovascular reactions.

Conclusion

To reduce the risk of cardiac rhythm disturbances and of an increase in blood pressure in the post-surgery period, patients with arterial hypertension, fatal ventricular arrhythmias and Amiodarone-associated type I thyrotoxicosis are recommended to take premedication with benzadiazepines in a prolonged course (Diazepam – three days before the surgery at night orally, 5–10 mg, and 1 hour before anesthesia, 0.5% solution at a dose of 0.15 mg/kg, i.m.) in combination with the introduction of 5 ml of 25% solution of magnesium sulfate.

At a sharp limitation in the timing of the patient's preparation for surgery, the appointment of long-acting benzodiazepines (Diazepam orally at night, 5–10 mg, and 1 hour before anesthesia at a dose of 0.15 mg/kg, i.m.) has advantages over short-acting benzadiazepines (Midazolam, 0.5% solution at a dose of 0.07–0.1 mg/kg, i.m., 40–60 minutes before anesthesia) due to the prevention of the development of life-threatening cardiac rhythm disturbances and an increase in blood pressure in the early post-surgery period.

The prolonged premedication with benzodiazepines and magnesium preparations in patients with arterial hypertension prevents the development of serious undesirable side reactions of the drug therapy for thyrotoxic syndrome and worsening of symptoms of the cardiovascular system.

Conflict of interests

The authors declare no conflicts of interests.

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