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The New Approach to Preventive Antiarrhythmic Therapies of Paroxysmal Tachycardias by Means of Electrophysiological Research of Heart

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Abstract

As many as 126 patients with paroxysmal tachycardia (PT) were surveyed. Depending on the way of selection of preventive antiarrhythmic therapies (AAT) the patients were divided into two groups, namely Group 1 and Group 2. Group 1 was the control group in which the treatment selected was a known method. AAT for Group 1 was appointed on the basis of an intravenous test during intracardiac electrophysiological investigation (EPI); for the per oral test the same preparation was performed the next day during transesophageal EPI (TEPI) by "saturation" of the preparation for 3 to 5 days. If it was not possible to induce a PT, treatment would be according to the intracardiac EPI. In Group 2 a selection of therapy was performed by an offered method. Etmozine, verapamil, propafenone, and quinidine were used for treatment of both groups. An advanced method of chronic intracardiac EPI, based on repeated induced PT and tachyarrhythmia with background per oral testing of AAT during their "saturation", allows to increase the efficiency of treatment in the remote period up to 98% and by an individual dose approach and the scheme of purpose of preparations which were found to correspond only in 47% of cases. The predictive criterion of the long-term efficiency of AAPs, revealed during their "saturation" in reciprocal orthodromic AV tachycardia (ROAVT) and reciprocal intranodal AV tachycardia (RIAVT), was the elimination of a zone of vulnerability or its acute reduction: for ROAVT, reduction of Wenkebach "point" to not less than 30 impulses per minute is necessary; for a tachycardia also with AF, elimination or acute reduction of a zone of vulnerability, along with increase of the ERP of AV connections in the antergrade direction and decrease of Wenkebach "point" to not less than 30 impulses per minute is required. For patients with ROAVT and AF, frequency of reproducibility of PT and tachyarrhythmia above the authentic level on performing intracardiac ECS, compared to TEPI, also does not differ for patients with RIAVT. IJBM 2011;1(2):74-78.

Key words: *paroxysmal tachycardia, transesophageal and intracardiac electrophysiological investigation.*

Introduction

Heart rhythm disturbance (HRD) has been one of the basic problems in modern cardiology until now. The medical and social value of this pathology is defined by significant prevalence, increase in the risk of sudden death, significant deterioration in the condition of the patient, complexity in diagnostics and increasing expenses in the treatment of patients with HRD [3].

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Treatment of paroxysmal tachycardia (PT) is now performed by means of medical products, electropulse therapy, and electrocardiostimulation (ECS), and also by catheter and surgical interventions [2, 7]. Medicamentous therapy continues to remain the basic method for antiarrhythmic influences. A variety of mechanisms, tachycardias, and various clinical and unequal sensitivities to antiarrhythmic preparations considerably complicate the selection of an adequate therapy and the estimation of its efficiency [8].

In a situation which is characterized by the application of a plenty of antiarrhythmic drugs and the development of new methods of endocardial influences on the pathways of the heart, the problems of an objective

estimation of the effect of a treatment are real such as studying preparations, and selecting and comparing various non-medicamentous approaches for the termination of PT and tachyarrhythmia.

To control the efficiency of the AAT, repeated EPI, ECG monitoring, transesophageal EPI, and tests of physical tolerance are now carried out. The most authentic monitoring of treatment quality is repeated EPI [5].

By means of EPI, in some cases it is possible to reveal AAT for arrythmogenic action. It has great value for patients and allows excluding similar medical drugs as their application can cause menacing, fatal aggravation of the prevailing PT [1, 9].

However, because of the complexity involved in implementation, the given method does not find a wide application in clinics. In the past years the method noninvasive TEPI [1, 4] had been widely introduced in clinical practice. Its efficiency in reproducing PT is 85–94% and according to S.P. Golitsin [9], HRD has been documented by monitoring the state of TEPI in 100% of the patients. Availability of a method enables the use of the same not only in selected AATs but also for the subsequent treatment controls [1, 4]. The opportunity of numerous repetitions of TEPI in a day allows the selection of a dose of antiarrhythmic preparation and the frequency rate of its reception [2, 4].

The purpose of the given research is the estimation of the clinical efficiency of an individual approach to AAT in patients with paroxysmal tachycardia (PT).

Methods

The criteria for inclusion in our research were various forms of documented PT. The criteria for exclusion were patients with unstable angina; acute myocardial infarction (MI) for less than 6 months; heart valvular diseases; presence of obstructive diseases of lungs; confirmed dysfunction of a thyroid gland; and also blood clots in the cavities of the heart revealed by transesophageal ultrasound research of the heart; and previous stroke. 126 patients were surveyed. Of them, 77 (61.1%) were women of ages ranging from 15 to 58 years (middle age 35.9±2.9 years). Duration of the arrhythmic anamnesis varied from 3 months to 11 years; frequency of occurrence of PT was 10.9±2.5 cases within duration of 0.25 to 30 hours (6.5±1.5 hour on average). During attacks of PT, the heart rate (HR) measured on the surveyed patients changed from 92 up to 160 (109.6±10.6 on average).

While the EPI was performed, reciprocal orthodromic AV tachycardia (ROAVT) was revealed in 40 (31.7%) patients; reciprocal intranodal AV tachycardia (RIAVT) in 37 (29.4%) patients; paroxysms of atrial fibrillations (AF) in 21 (16.7%) patients; paroxysms of atrial flutter (AFl) in 3 (2.4%) patients; ventricular tachycardia (VT) in 5 (3.9%) patients; a combination of ROAVT and AFl was revealed in 14 (11.1%) patients; and a combination of RIAVT and AFl in 6 (4.7%) patients. In all patients, PT was accompanied by symptoms of heart failure (HF). Before admission to a hospital all patients received a wide spectrum of antiarrhythmic preparations (AAP) (from 2 up to 6) lasting for not less than 4 weeks in adequate recommended doses [2].

Based on the method of selection of preventive AAT, the patients were divided into two groups: Group 1 in which selection of treatment was performed by a known method. AAT for patients of Group 1 was appointed on the basis of an intravenous test during intracardiac EPI; for the per oral test the same preparation was performed the next day during TEPI by "saturation" of the preparation for 3–5 days. If it was not possible to induce PT, the treatment was by intracardiac EPI. In Group 2 selection of therapy was performed by an offered method. For both groups etmozine, verapamil, propafenone, and quinidine were administered. The long-term effect of the treatment was estimated by questioning the patients, interrogation by phone, and repeated surveys [3].

Results

The results obtained after inducing PT and tachyarrhythmias were analyzed by TEPI and were compared with those conducted by intracardiac EPI on 63 patients. As a whole, intracardiac EPI was carried out on 58 (92%) and TEPI on 43 (69%) at various times. This distinction did not appear to be significant. At the same time, by analyzing separate forms of HRD, it was possible to establish that ROAVT and AF are induced authentically more often by performing intracardiac EPI ($p<0.05$ and $p<0.01$) than by TEPI. It was possible to induce VT only on one of two patients by carrying out intracardiac EPI and TEPI by speeding up the stimulation of auricles. Besides, it was observed that diagnostic intracardiac EPI repeatedly caused HRD in both methods of research. In a unique case when results of intracardiac EPI and TEPI did not coincide, at the AV-nodal tachycardia, it was assumed to have been caused by endocardiac stimulation only from the right ventricle [8]

We compared the electrophysiological parameters of 23 patients on whom intracardiac EPI and TEPI were simultaneously performed. For this purpose, during intracardiac EPI and TEPI an electrode was added in a gullet and alongside with the program, diagnostic endocardial ECS was performed in parallel with the program of transesophageal ECS.

By simultaneously performing TEPI and intracardiac EPI, the authentic distinctions in effective refractory period (ERP) of the left auricle ($p<0.005$) and AV node ($p<0.03$) were observed. After introducing preparations, these distinctions disappeared except for "a zone of vulnerability". According to intracardiac EPI, after the introduction of the antiarrhythmic drug it was maintained in 4 out of 23 patients, whereas by TEPI only in 2. Thus, duration of TEPI in both cases made "zones of vulnerability" of 20 ms and by intracardiac EPI 30 ms and more. Thus, the results obtained allow the assumption of the following:

1. Chances of provoking ROAVT and AF by intracardiac EPI are more compared to TEPI. This fact should, most likely, be considered as an estimation of the efficiency of AAT as, probably, the positive results of TEPI will more adequately predict the prevention of long-term therapy compared to intracardiac EPI.

2. The performance of intracardiac EPI and TEPI at various times authentically reduces the uniformity of modeling of the same HRD.

Method of approach to preventive AAT based on chronic EPI

An estimation of the preparations of AAE by means of programmed ECS during "saturation" by a medicine was done by using the standard scheme of AAT: average daily doses of preparations were given in 3 to 4 receptions. In such an approach, there are unresolved following questions as to the choice of treatment: what optimum unitary effective dose should be administered to each patient? What duration of action of a unitary dose of a preparation and how often should it be administered in a day? The most convenient method in the selection of AAT was the method of chronic intracardiac EPI because TEPI was less authentic and its application in some of the patients was limited because of a painful syndrome. The method of approach of the AAT consisted of the following: at the first stage ECS which steadily provoked PT, was spontaneously identified. Then per oral test was introduced in one of the AAP at an average therapeutic dose whose choice was based on the results of a medical test or a previous preventive treatment. Then ECS in the picked up modes was repeated every 30 to 40 minutes after reception of a preparation. In cases, if it was not possible to provoke a PT, this AAP was considered to be effective to the given patient. Continuously carrying out ECS at specified time intervals, the moment when PT was provoked again was identified. Thus, for each patient the time of beginning and ending of preparation after its unitary reception was established to be within 30 to 45 minutes was established.

In the following stage, unitary dose-effective dose preparations were established. AAE was acknowledged by repeated ECS on a half dose of a preparation and was considered optimum for preventive reception. In cases of PT provoked after 2 to 3 x hours after reception of an average therapeutic dose of the chosen preparation, the second dose of preparation was administered exceeding the initial by 1.5 to 2 times and the ECS procedure was repeated. In the subsequent provoked PT, this AAP was considered inefficient. When a distinct preventive action of a preparation was achieved at such an increase in dosage, the time of approach and the termination of effect were estimated.

The third stage consisted of an estimation of the efficiency of the picked up preparation and its dose during "saturation" by the technique described above. Reduction of validity increased the periodicity of reception of the same dose in a day by 1 to 2 times. An increase in the validity of a preparation reduced the number of receptions.

The estimation of a long-term efficiency of AAT was performed by the following criteria: a full termination of relapse of the PT by supporting the AAT in the background was considered to be good; a significant (more than on 50 %) reduction in number and duration (no more than 15 to 20 minutes) of PT and a spontaneous terminating of the AAE was considered satisfactory. All other cases were considered to be negative.

For the treatment, etmozine, verapamil, propafenone, and quinidine were applied. In total, out of 63 patients, the preventive treatment by the offered method was applicable only in 59 (94%) patients. Only 87 of the AAPs were effective. Of them, 18 were not applicable for long reception as the duration of action of a unitary dose of the preparations did not exceed 4 hours.

On the whole, the AAT has appeared to be effective in all patients although 5 patients received a correction of treatment; 3 developed side effects due to etmozine; and 2 developed tachyphylaxia.

Unitary effective doses of the same preparations differed for different patients. For etmozine, verapamil, propafenone, and quinidine the difference between the minimal and maximal effective doses was 300% and for verapamil it was 500%. On average, the therapeutic dose used in preparations was effective only in 34 out of 69 cases, which is less than half (49.3%).

There was considerable difference in the terms of the beginning and duration of action of the same preparations in different patients. So, the etmozine began to act in 30 to 120 minutes (70.2±2.8 minutes on average), and duration of its action ranged between1 and 16 hours (4.5±6.2 hour on average). Verapamil also started to act in 30 to 120 minutes (55.2±4.2 minutes on average) and AAE was maintained from 1 hours to 12.5 (7.2±2.6 hours on average). Within the same terms, in 30 to 120 minutes (55.2±3.6 minutes on average) the action of propafenone, which proceeded from 2.5 to 18 hours (9.2±2.7 hours on average), was shown. The beginning of action of quinidine in some patients was tightened at 2.5 to 3 hours, and thus duration of its action was between 6 and 20 hours (8.1±12.4 hour on average).

Dependencies on the duration of action of a preparation from its dose and time of taking effect have not been revealed.

The analysis of long-term efficiency of AAT based on electrophysiological parameters of heart

Analysis of the changes in the electrophysiological parameters of the heart was performed in 59 patients who had received the recommended treatment for 12 months. For defining the criteria of efficiency of the AAT we considered the ERP of the right auricle, ERP of the A-V node in the ortho- and antidrome directions, Wenkebach "point", and duration of a zone of vulnerability [5]. Unsatisfactory results of the treatment obtained during chronic EPI were not taken into account; on the other hand, the good and satisfactory results were compared. Patients with both ROAVT and a combination of RIAVT, AF, and AFl were included in the analysis. From the data received (tabl.1), it was observed that an authentic distinction in the changes in the electrophysiological parameters of the two groups of patients during "saturation" by a preparation is only the presence or absence of a zone of vulnerability and its duration. In patients with RIAVT, an authentic predictive criterion of efficiency of preventive AAT with the impossibility of inducing AF and a disappearance of a zone of vulnerability was evident [2].

It is also important to consider by such an electrophysiological parameter, as reduction of Wenkebach "point" in the antergrade direction is not less than on 30 impulses in a minute. By flutter-fibrillation of auricles an additional criterion was the disappearance of the ERP difference between the auricles.

Table 1
Individual changes of distinctions of electrophysiological parameters of the heart up to and during "saturation" by a preparation in patients with atrial fibrillation and flutter with different preventive effect of treatment

Parameters of EPI	Effect of therapy			
	Good (n=11)		Satisfactory (n=10)	
	Background	Under action of a preparation	Background	Under action of a preparation
ERP of RA , ms	198±9.36	274±53.2	214±8.9	263±15.2
	uncertain		p <0.01	
ERP of LA, ms	264±16.5	277±37.1	244±21.4	267±17.2
	uncertain		uncertain	
Difference ERP of RA and LA, ms	64±7.1	5±1.3	52±9.8	6±3.4
	p <0.05		p <0.05	
ERP of AV-node, ms	242±18	268±67.9	232±14.6	267±17.2
	uncertain		uncertain	
"W-point", imp/min	170±14.1	141±13.3	231±13.5	190±10.4
	uncertain		p <0.03	
Duration of a zone of "vulnerability", ms	61.4±17.3	2.3±1.2	44.2±7.5	4.6±2.9
	p <0.01		p <0.003	

Notes: *ERP – effective refractory period, EPI – electrophysiological investigation, LA – left atrium, RA – right atrium, "W-point" – Wenkebach point*

Comparison of efficiency of long-term AAT which has been compared to different methods

It is found that long-term efficiency of the preparations which have been picked up in the offered way, it is authentic above ($p<0.05$), than at known. At the same time for one of preparations of an authentic difference between two groups it is not received, obviously, because of a small amount of supervision.

The amount of complications and the collateral actions of the preparations, because of which we have been compelled to cancel treatment, in the first group of patients was 7% more ($p<0.05$) compared to the second. A development of tolerance to preparations was noticed in only one case when an increase in a dose of verapamil at 50% was required by a patient of Group 2.

In prospective supervision of empirically appointed doses and the scheme of reception of preparations (after acknowledgement of their positive action in acute medical test and during "saturation") the effect changed from unsatisfactory to good in 3 out of 4 patients, to good in 1, and to satisfactory in 2 patients. In 3 patients a change of dose and periodicity of reception of medicines resulted in a change from satisfactory to good. One patient continued to have a satisfactory result of therapy even after a change of the scheme of treatment, but on average ROAVT has decreased by 30% a month at simultaneous reduction of its average duration by 50%. Thus, in 7 out of 10 cases, individual approach to AAT has allowed to increase the efficiency of the treatment by the same preparations which were appointed earlier on the basis of the method described in the literature [1].

Finally (that is for all periods of supervision), an absolute AAE of the treatment in 12 to 60 months was observed in 33 out of 59 (56 %) patients; in others it was satisfactory. In Group 1, among 41 patients good AAE was observed in 10 (24%), and in others a reduction in number and/or duration in PT was ascertained. A distinction (of 32%) in good or satisfactory result of treatment between these groups has appeared to be statistically significant ($p<0.05$).

It is established, that updating of a known way of selection of preparations authentically raises the efficiency of long-term treatment if the opportunity of PT prevention during "saturation" by a medicine is proved. Thus, dependencies of the long-term effect of treatment on the character of the basic disease, the form of HRD, a degree of insufficiency of blood circulation, PT frequency, sex, and age of the patient are not revealed.

Conclusions

1. An advanced method of chronic intracardiac EPI, based on repeated induced PT and tachyarrhythmia by background per oral testing of AAT during their "saturation", allows to increase the efficiency of the treatment in the remote period up to 98% and by an individual dose approach and the scheme of purpose of preparations which were found to correspond only in 47% of cases.
2. The predictive criteria of the long-term efficiency of AAP, revealed during their "saturation" in ROAVT and RIAVT, is the elimination of a zone of vulnerability or its acute reduction: for ROAVT, reduction of Wenkebach "point" of not less than on 30 impulses per minute is necessary; for a tachycardia also at AF, elimination or acute reduction of a zone of vulnerability, along with

increase in the ERP of AV connections in the antergrade direction and decrease in Wenkebach "point" of not less than 30 impulses per minute is required.

3. For patients with ROAVT and AF, the frequency of reproducibility of PT and tachyarrhythmia above the authentic level on performing intracardiac ECS, compared to TEPI, also does not differ for patients with RIAVT.

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