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ТИББИЁТДА ЯНГИ КУН НОВЫЙ ДЕНЬ В МЕДИЦИНЕ NEW DAY IN MEDICINE

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METHODS OF PREVENTION AND TREATMENT OF ATRIAL FIBRILLATION

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✓ Resume

Atrial fibrillation (AF) is the most common heart rhythm disorder requiring treatment. The key points of treatment include relief of paroxysmal AF and planned antiarrhythmic therapy. The article provides a brief overview of the main antiarrhythmic drugs used to relieve paroxysms of AF and for planned maintenance of sinus rhythm. Unique in this series is propafenone, available in two forms - oral and intravenous, which makes it a therapeutic agent at all stages of stopping paroxysmal AF and for planned antiarrhythmia.

Key words: planned antiarrhythmia, atrial fibrillation, relief of paroxysm of atrial fibrillation.

МЕТОДЫ ПРОФИЛАКТИКИ И ЛЕЧЕНИЯ ФИБРИЛЛЯЦИИ ПРЕДСЕРДИЙ

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✓ Резюме

Фибрилляция предсердий (ФП) – наиболее распространенное нарушение сердечного ритма, требующее лечения. К ключевым моментам лечения относятся купирование пароксизма ФП и плановая антиаритмическая терапия. В статье представлен краткий обзор основных антиаритмических препаратов, применяемых для купирования пароксизмов ФП и для планового удержания синусового ритма. В этом ряду уникальным является пропafenон, доступный в двух формах – пероральной и внутривенной, что позволяет лечебным средством на всех этапах купирования пароксизма ФП и при плановой антиаритмии.

Ключевые слова: плановая антиаритмия, фибрилляция предсердий, купирование пароксизма фибрилляции предсердий.

АРТЕРИАЛ ФИБРИЛАЦИЯНИ ОЛДИНИ ОЛИШ ВА ДАВОЛАШ УСУЛЛАРИ

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✓ Резюме

Артериал фибриляция (АФ) даволанишни талаб қиладиган энг кенг тарқалган юрак аритмияси ҳисобланади. Даволашнинг асосий нуқталари АФ пароксизмини енгилаштириш ва режалаштирилган антиаритмик терапияни ўз ичига олади. Мақолада АФ пароксизмларини енгилаштириш ва sinus ритмининг режалаштирилган ушлаб туриш учун ишлатиладиган асосий антиаритмик дорилар ҳақида қисқача маълумот берилган. Пропафенон ушбу серияда ноёбдир, икки шаклда мавжуд – оғиз орқали ва томир ичига юборилади, бу даво востасини АФ пароксизмини енгилаштиришнинг барча босқичларида ва режалаштирилган антиаритмик даво пайтида ишлатишга имкон беради.

Калит сўзлар: режали антиаритмия, атериал фибриляция, атериал фибриляция пароксизмида ёрдам.

Relevance

Atrial fibrillation (AF) is the most common heart rhythm disorder found in 1-2% of the adult population of the earth. The key issues in the treatment of AF are anticoagulant, planned antiarrhythmic or pulse-reducing therapy and restoration of sinus rhythm in AF paroxysm. The article examines the issues of antiarrhythmic therapy.

Relief of atrial fibrillation paroxysm in the first place, with AF paroxysm, the doctor must decide whether it is advisable to restore the sinus rhythm and, if the decision is positive, choose a method for its restoration.

Decisions on the relief of atrial fibrillation paroxysm

When deciding on the relief of AF paroxysm, the doctor should be guided by the following considerations: 1) the presence of complications associated with paroxysm; 2) the probability of maintaining a sinus rhythm after recovery; 3) the patient's tolerance of arrhythmia. If AF paroxysm leads to life-threatening complications for the patient: acute coronary syndrome, acute heart failure, clinically significant hypotension (blood pressure - BP), let's take a closer look at these recommendations. We should divide all patients with AF paroxysms into 2 groups: with and without severe organic heart lesions. According to experts, in relation to the relief of AF, we should attribute to severe organic heart lesions the unstable course of coronary heart disease (CHD), a marked decrease in systolic function of the left ventricle (LV) [ejection fraction (EF) 14 mm. In these situations, class 1A and 1C drugs (propafenone, procainamide) cannot be used [1,3,4]. At the same time, with pronounced organic lesions of the heart, the expediency of restoring the sinus rhythm is generally questionable, especially at the prehospital stage. If the AF paroxysm proceeds without significant complications, the issue of maintaining arrhythmia and conducting pulse-reducing therapy should be resolved. In patients with complicated AF, EC is the optimal choice. In this situation, anticoagulant therapy should be initiated as soon as possible to prevent normalization of embolism [2,5,6]. Anticoagulant therapy should begin with the appointment of low molecular weight heparin (LMH), for example enoxaparin, in combination with warfarin or new oral anticoagulants (NOAC): dabigatran etexilate, rivaroxaban or apixaban. LMH is canceled only after achieving the target INR of 2.0 to 3.0 in two consecutive analyses on warfarin therapy, which confirms the beginning of the effective action of warfarin. Due to the rapid onset of action, when prescribing NOAC, the paravenous administration of LMH is not required. If the patient is in a stable condition, a medical cardioversion is performed. If the duration of AF paroxysm is over 48 hours, it is possible to restore the sinus rhythm only in patients who are taking anticoagulant drugs on a planned basis [7,8].

Drug-induced cardioversion Schemes for the relief of AF paroxysm at the prehospital stage and in the hospital, presented in the National Guidelines for the treatment of AF [9]. Let's take a closer look at these recommendations. We should divide all patients with AF paroxysms into 2 groups: with and without severe organic heart lesions. According to experts, in relation to the relief of AF, we should attribute to severe organic heart lesions the unstable course of coronary heart disease (CHD), a marked decrease in systolic function of the left ventricle (LV) [ejection fraction (EF) 14 mm. In these situations, class 1A and 1C drugs (propafenone, procainamide) cannot be used. At the same time, with pronounced organic lesions of the heart, the expediency of restoring the sinus rhythm is generally questionable, especially at the prehospital stage. If the AF paroxysm proceeds without significant complications, the issue of maintaining arrhythmia and conducting pulse-reducing therapy should be resolved. In patients with complicated AF, an ECG is the optimal choice. The use of amiodarone at the prehospital stage is ineffective due to the delayed action of the drug. In this situation, the use of propafenone is practically no alternative due to the solid evidence base confirming the high level of efficacy and safety. And the presence of two forms – oral and intravenous – makes it possible for the patient to use the drug independently ("tablet in his pocket"), by an outpatient doctor or an ambulance. Intravenous administration of the drug allows you to get a faster result compared to the oral form. With intravenous administration, it usually takes from 30 minutes to 2 hours to restore the rhythm, when taking the drug orally at a dose of 450-600 mg – 2-6 hours. The effectiveness ranged from 41 to 91% [1]. The drug should not be prescribed to patients with severe LV dysfunction (LV 14 mm) and unstable coronary heart disease. Propafenone has weak β -adrenoblocking activity, therefore it is advisable to avoid its use in patients with severe bronchial obstruction [2,10].

According to the results of small studies, the effectiveness of procainamide in eliminating a recent attack of AF is low – about 40-50% in the first 8-12 hours after its administration and does not significantly differ from placebo [1,4,7]. The drug is not used for the relief of AF in Western Europe and North America. In addition, intravenous administration of the drug is often complicated by hypotension, which requires, from our point of view, limiting the use of this drug; propafenone should replace it. Amiodarone has a pronounced

but delayed effect in the relief of AF, which makes it inappropriate to use it at the prehospital stage of treatment. In the first hours, only the beta-adrenoblocking effect of the drug is realized. The antiarrhythmic effect increases during the day. Amiodarone is administered intravenously at a dose of 5 mg / kg for an hour (300-450 mg / h), then 50 mg / h (1000-1200 mg per day). The daily dose should not exceed 1200 mg. Amiodarone should not be mixed with other drugs or other drugs should be administered simultaneously through the same venous access. The drug is administered only in diluted form and only in 5% glucose solution. The drug often causes phlebitis. Nitrophenyldiethylaminopentylbenzamide (nibentane)[®] is a natural drug that is not registered in Western Europe and America. According to National recommendations, it can be used as a means of medical cardioversion, including in the presence of structural heart disease, if LVEF is >40%, including with persistent arrhythmia. Serum electrolyte levels and the QTc interval should be within the normal range (ardia (Torsades de pointes), according to various data, can occur in 3-12% of cases (5,6,8). Thus, from our point of view, the risk of using the drug is too high for its widespread use. EC is more effective and safe and does not require long-term monitoring of the patient after restoration of the sinus rhythm. The doses of antiarrhythmic drugs for the relief of AF paroxysms are presented in Table 1

Table 1. Doses of antiarrhythmic drugs for the relief of atrial fibrillation paroxysms [6]

Medicaments	Doses
Procainamide	500-1000 mg for 15-20 minutes under blood pressure control
Propafenone	450-600 mg orally once (maximum daily dose 900 mg) or 2 mg / kg intravenously (4 ampoules – 140 mg) for 10-15 minutes. Repeated intravenous administration is possible after 90-120 minutes (the maximum daily dose for intravenous administration is 560 mg)
Amiodarone	5 mg / kg (300 mg) for 15-20 minutes. Further drip administration: 360 mg / 6 h, 540 mg / 18 h (maximum daily dose – 1200 mg)
Nitrophenyldiethylaminopentylbenzamide	0.065–0.125 mg / kg intravenously for 3-5 minutes. If there is no effect, repeated infusions at the same dose with an interval of 15 minutes (up to a total dose of 0.25 mg / kg)

Allapinin, etacizine, sotalol, which are used as planned to maintain sinus rhythm, are not recommended for the relief of AF paroxysms [3]. If antiarrhythmic drugs are ineffective, the method of choice is EC, the effectiveness of which exceeds 90% [2,9].

SELF-TREATMENT OF ATRIAL FIBRILLATION PAROXYSM BY A PATIENT - "A PILL IN YOUR POCKET"

The issue of restoring the sinus rhythm in AF paroxysm is extremely important, as this leads to emergency calls, an increase in the frequency of hospitalizations and, as a result, a decrease in the quality of life. However, it is possible to restore the sinus rhythm on an outpatient basis and at home, using the "pill in your pocket" tactic. The only drug in Russia recommended as a "pill in your pocket" is propafenone. The cupping effect of the drug develops within 2-6 hours after taking it [1], and this is very convenient when used on an outpatient basis or at home. Important data on the use of propafenone were obtained in Russian studies that confirmed the high efficacy and safety of the drug in the relief of AF paroxysms [1]. The first use of the drug is recommended under the supervision of a doctor [2, 5]. The results of a Russian study [7] showed that the effectiveness of 600 mg of propafenone in the relief of AF paroxysms was 84%. The high safety of the drug in a wide category of patients was also shown in the Russian study PROSTOR [1]. The drug Propanorm[®] ("PRO.MED.CS Praha a.s.") was used in the studies. According to the data provided in the Russian recommendations for the treatment of AF, the effectiveness of propafenone in relieving AF paroxysm varies from 41 to 91% [2]. P. Alboni et al. [8] the effectiveness of propafenone is estimated at 94%, provided that

the drug is used early. In this study, the average time of taking the drug after the onset of AF paroxysm was 36 minutes [6]. My own experience of using propafenone (Propanorm) for 5 years in a hospital with ECG monitoring in 106 patients did not reveal any clinically significant proarrhythmic effect. Isolated cases of bradycardia were temporary, clinically insignificant and did not require treatment. Examples of sinus rhythm restoration during ECG monitoring are shown in Fig. 3. Based on the above, the following protocol for the use of propafenone in patients with AF can be used. The conditions for restoring sinus rhythm with AF paroxysm in outpatient settings using propafenone are the duration of AF <48 hours or constant intake of warfarin with INR 2.0–3.0 or NOAC (dabigatran etexilate, rivaroxaban or apixaban). There should be no irreversible causes of AF or a complicated course of paroxysm. The availability of data on the effectiveness of antiarrhythmic therapy in previous sinus rhythm restorations is an additional argument in favor of interrupting AF paroxysm.

Table 2. The main antiarrhythmic drugs used for the planned therapy of atrial fibrillation

Medication	Moderate daily dose	Features of the drug
Metoprolol succinate	50-200 mg in 1 or 2 doses	Is inferior in effectiveness to other antiarrhythmic drugs. The drug of choice for severe organic heart disease, severe chronic heart failure
Propafenone	150 mg 3 times, 300 mg 2 times	Should not be used in severe organic heart disease. It is the drug of choice for moderate LV hypertrophy (≤ 14 mm). It can be used with stable coronary heart disease; in this situation it is better to combine with beta-blockers
Diethylaminopropionylethoxy carbonylaminophenothiazine a hydrochloride	50 mg 3 times	Should not be used in severe organic heart disease
Sotalol	80-160 mg 2 times	Should not be used in severe organic heart disease
Amiodarone	200 mg 1 time	Can be used in patients with severe organic heart disease. Due to a number of severe extra-cardiac complications, it is a reserve drug
Dronedarone	400 mg 2 times	Should not be used in severe organic heart disease. It is inferior in effectiveness to other antiarrhythmic drugs. High price

SCHEME FOR THE RELIEF OF ATRIAL FIBRILLATION PAROXYSM IN a polyclinic

1. ECG to confirm AF, assessment of the corrected Q–T interval (<460 ms)
 2. Propafenone (propanorm®) 600 mg once at a body weight of 70 kg and above, if the body weight is < 70 kg – 450 mg (1, 7, 9).
 3. Observation in a day hospital for 4 hours.
 4. When the sinus rhythm is restored, repeated ECG removal, blood pressure monitoring.
 5. If the AF paroxysm is not stopped, decide on further tactics: hospitalization to restore sinus rhythm in a hospital or the appointment of pulse-reducing therapy.
 6. Assessment of the risk of thromboembolic complications on the CHA2DS2 VASc scale. Prescribing anticoagulants if the risk is 1 point or more.
 7. Assessment of the risk of hemorrhagic complications on the HAS BLED scale. With a risk of 3 points or more, it is necessary to adjust treatment tactics, for example, prescribe anti-ulcer therapy or cancel drugs that increase the risk of bleeding.
 8. In a stable condition, the patient leaves the clinic with a second consultation with a cardiologist the next day to resolve the issue of planned antiarrhythmic and anticoagulant therapy.
- At home 1. Strict bed rest for 6 hours 2. Monitor blood pressure and heart rate (HR) before taking the drug. With a heart rate <70 per minute and blood pressure < 110/70 mmHg, taking the drug is not

recommended. 3. Take 300 mg of propafenone (propanorm®). 4. After 1 hour, blood pressure and heart rate control. 5. If the sinus rhythm does not recover, and blood pressure and heart rate indicators meet the above criteria, take another 300 mg of propafenone. 6. If the AF paroxysm is not stopped within 6 hours, you should consult a doctor to determine further treatment. 7. With the effectiveness and good tolerability of the drug, a single dose of propafenone (propanorm®) at a dose of 600 mg is recommended in the future to relieve AF paroxysm. Attention is drawn to the need to monitor blood pressure and heart rate and to observe bed rest after taking the drug.

INDICATIONS FOR MANDATORY HOSPITALIZATION IN CASE OF ATRIAL FIBRILLATION PAROXYSM

1. The first recorded paroxysm of AF.
2. The development of complications (anginal pain, ECG ischemia, heart failure, neurological symptoms, etc.).
3. Heart rate >150 per minute In other cases, it is possible to restore the sinus rhythm on an outpatient basis.

CONTRAINDICATIONS FOR THE USE OF PROPAFENONE

1. Marked decrease in LV systolic function (LV >14 mm).
2. Unstable course of coronary heart disease.
3. Pronounced LVH (>14 mm)
4. ECG prolongation of the corrected Qt interval >460 ms.
5. Sinus node dysfunction.
6. Conduction disturbances.
7. Bronchoobstructive diseases.
8. Glycoside intoxication. The above protocol has been used in our center for outpatient patients for more than 3 years.

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