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Bogomolets National Medical University

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Department of Clinical Pharmacology and Clinical Pharmacy

GRADUATE MASTER'S THESIS

Topic: «RISK MANAGEMENT OF MACROLIDE USE IN PATIENTS WITH CARDIAC ARRHYTHMIA»

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LIST OF CONDITIONAL ABBREVIATIONS

ECG	Electrocardiography
AH	Arterial hypertension
BA	Bronchial asthma
HR	Heart rate
AF	Atrial fibrillation
SA node	Sinoatrial node

INTRODUCTION

Actuality of theme.

Violation of the heart rhythm is a violation of the conduction or occurrence of an electrical impulse in the heart muscle. Arrhythmias can occur with pathology of the sinoatrial node, with organic damage to the myocardium, with somatic diseases of other organs. The impetus for the development of arrhythmia can even be the influence of external factors.

The following types of arrhythmia are distinguished:

1. Sinus arrhythmia
2. Paroxysmal arrhythmia
3. Atrial fibrillation
4. Ventricular arrhythmia.

The main threat of arrhythmia is myocardial overload with a high risk of developing heart failure. Hypertrophy and dilatation of heart cavities can develop, valve pathology occurs, primarily mitral and aortic. Atrial fibrillation occurs more often in elderly patients who have several concomitant diseases. However, the development of arrhythmia may be associated with an undesirable drug interaction with the simultaneous use of two drugs with a cardiotoxic effect. Or in the treatment of a patient with impaired conduction or with congenital defects of the conduction system of the heart or other pathological conditions of the myocardium or the conduction system with the use of drugs with cardiotoxicity.

Patients of any age may be at risk of developing acute bacterial infection of the soft tissues, respiratory system, genitourinary tract, muscles, and skin, requiring antibacterial therapy. Antibiotics of different groups are used to select adequate antibiotic therapy, some of them show cardiotoxicity. In recent years, allergic reactions to antibacterial drugs from the group of penicillins and cephalosporins often occur, which causes the doctor to choose a drug from the group of macrols.

The purpose of the work:

To determine the risk management of the use of macrolides in patients with heart rhythm disorders.

Task:

1. To determine risk factors for the development of complications of macrolide treatment in patients with heart rhythm disorders.

2. To analyze the frequency of risks of developing unwanted drug interactions in patients with heart rhythm disorders when using macrolides.

3. Develop recommendations for the pharmacotherapy of patients with heart rhythm disorders when using macrolides.

Research Methods: Analytical (analysis of disease histories).

Scientific novelty.

The risk of drug interaction in patients with heart rhythm disorders during treatment with antibacterial drugs of the macrolide group was assessed.

An algorithm for effective and safe macrolide treatment of patients with heart rhythm disorders has been developed.

The practical significance of the results obtained.

Results obtained regarding the risks for cardiac arrhythmia patients taking macrolides.

Structure of work:

The total number of pages is 59;

Number of chapters – 3;

Number of applications – 0;

The number of sources used is 62.

CHAPTER 1

LITERATURE REVIEW

1.2. Disturbance of the heart rhythm

Every year, more and more sweet people fall ill with the pathology of the cardiovascular system. The problem of cardiovascular diseases is a big medical and social problem. Mortality is 64% from diseases of the heart and blood vessels [1].

This encourages the diagnosis, prevention, and treatment of cardiac diseases. In cardiology, the results of evidence-based medicine are used [2].

One of the diseases is cardiac arrhythmias. Arrhythmology is a complex clinical discipline, the treatment of heart conduction and rhythm disorders is constantly being improved. Treatment recommendations are reviewed annually

Invasive methods of treating arrhythmias are actively developing [3].

There is a classification of diseases. Cardiac arrhythmia according to the classification of diseases has the code I47 — I49. Arrhythmia is a change in the rhythm of the regular heart. The change in the heart rhythm is of different nature: pathological slowing of the heart rate and to excessive acceleration of the heart rate. There may also be asynchronous contraction of the atria or asynchronous contraction of the ventricles. There may be irregular heartbeats and heart skips.

Physiological control is automatically carried out in the heart in the absence of external stimuli. This ensures chronotropic coordination of contractions.

The center of first-order automatism is the sinoatrial node. The cells of the sinoatrial node have a high rate of diastolic depolarization and automatic activity due to the different permeability of cell membranes for Na+, K+, Ca, Cl [4, 5].

The centers of automaticity of the second and third order are the atrioventricular junction (from 30 to 40 per 1 minute) and the lower part of the bundle of His and Purkinje fibers (from 15 to 20 per 1 minute) [6].

The electric wave that arose in the sino-atrial node penetrates the myocardium of the atria and ventricles along the conduction system of the heart [7].

The cardiac conduction system has differences in morphology and function:

1. sinus-atrial node, sinoatrial node

2. interatrial and internodal conduction pathways (anterior – Bachman, posterior – Thorel and middle – Wenckenbach)

3. atrioventricular node (atrioventricular or Ashoff-Tavar node

4. bundle of His, the right and left legs of the bundle of His (to each ventricle), the left leg of the bundle of His has anterior and posterior branches;

5. Purkinje fibers are subendocardial

In addition, there are additional leading pathways of the heart:

- James
- Paladino-Kenta
- Mahaima and others.

From the atrium, the impulse spreads through them, bypassing the atrioventricular node without a physiological delay (0.12-0.18 seconds) in the node. This can be the cause of arrhythmia.

Additional conduction paths (for example, Paladino-Kent) are the cause of reciprocal, orthodromic atrioventricular tachycardia - the impulse goes to the ventricles in the usual way. The retrograde impulse goes through an additional conduction path. It can be antidromic, the impulse goes to the ventricles through additional pathways, and returns via the main pathway.

The sinus node is 2-6 mm in size, located at the confluence with the right atrium of the superior vena cava subepicardially. Blood supply by the right coronary artery. Branches of the vagus nerve innervate.

The atrioventricular node is located in the right atrium, in the lower part. Forms an atrioventricular connection together with the trunk of the bundle of His. The trunk of the bundle of His consists of three different histological parts. This is

the nodal part (the node itself), the atrial-nodal part (transitional), and the nodal-bundle part.

The atrioventricular node has important functions:

1. pulse delay of 0.12–0.8 seconds. This time is necessary for the contraction of the atria. Blood enters the ventricles. The P-Q interval is recorded on the ECG

2. conduction of bioelectric impulses from the atria to the ventricles;

3. the atrioventricular node becomes the pacemaker when the function of the sinus node is impaired

4. the atrioventricular node protects the ventricles from an excessive number of impulses from the atria in the event of atrial tachyarrhythmias. This is possible due to functional atrioventricular block.

The atrioventricular node consists of α- and β-fibers that have the ability to conduct impulses at different speeds. α- and β-fibers form two bundles with different speeds of electrical impulse conduction. The α-beam has a shorter refractory period and a lower conduction velocity than the β-beam. Longitudinal dissociation occurs and this may be the cause of reciprocal atrioventricular nodal tachycardia. Fast-slow and slow-fast tachycardia. The impulse passes through the β zone from the atria to the ventricles, can return through the α zone retrogradely and vice versa.

The length of the bundle of His is 10 mm. His right and left legs are the center of third-order automatism. The legs of the bundle of His conduct an impulse at a speed of 3–4 m/s. This ensures simultaneous excitation of all cells of the ventricular myocardium.

The connection of the conduction system of the heart with the fibers of the myocardium is carried out through the branching of Purkinje fibers subendocardially. The propagation of excitation occurs through the nexus, which contain ion channels. The propagation of impulses through the conduction system of the heart is 5 times greater than through the myocardium.

The unidirectional movement of ions through the protoplasmic membrane of cardiomyocytes leads to the emergence of electrical potentials in the myocardium.

in a non-excited state In the middle of the cell during diastole, the concentration of K+ is 30 times higher than outside the cell. 20 times higher than Na+. 25 times higher than Ca 2+ outside the cell [8].

The difference in concentrations is supported due to the active function of ion channels for the entry of Ca 2+, Na+, Cl–. After that, K+ comes out of it. This is done with the help of energy resulting from the breakdown of ATP with the participation of K+- and Na+-ATP-az [9].

The resting transmembrane potential difference is 90 mV. Spontaneous diastolic depolarization is the ability of a cell to depolarize spontaneously.

Spontaneous depolarization of sinus node cardiomyocytes generate cyclic bioelectrical impulses. These impulses spread along the conduction system of the heart.

Cardiomyocytes, spontaneously depolarizing, cyclically generate bioelectrical currents that spread through the conduction system of the heart. For individual ions, the permeability of the cell membrane changes during cell excitation. A transmembrane action potential curve is formed during graphical registration [10].

Action potential has 4 phases.

Phase 0. Cell depolarization. Fast sodium channels of the sarcolemma are activated. Na+ enters the cell. In 10 ms, a rapid depolarization of the cell membrane occurs. The cellular electrical charge changes to +20 mV from -90 mV. The period from 0 to +20 mV is called overshoot. A period of very rapid depolarization

Phase 1. Phase of early rapid repolarization. The polarity of the cell membrane in the atria is restored. Cl– ions quickly enter the cell. The membrane charge drops to 0 mV. Even below 0 mV.

Phase 2. Slow process of repolarization. A plateau appears on the transmembrane potential curve. The constant entry of slow Ca2+ and partly Na+ into the middle of the cell maintains a constant level of the action potential. Phase 2 lasts 200 ms. The ventricles contract. Blood enters the vessels.

Phase 3. Rapid repolarization of cardiomyocytes. K+ is released into the extracellular fluid, the polarity of the cell membrane is restored.

Phase 4. Heart diastole. Potential level -80 ... -90 mV. K+ leaves the cell, the resting potential in pacemaker cells decreases. This is the phase of diastolic spontaneous depolarization. The curve decreases to the initial level. Then the permeability of the membrane for Na+ increases sharply again, the cardiac cycle repeats.

There are several causes of arrhythmia development [11, 12]:

- Violation of the conduction of an electrical impulse — from the atrium to the ventricles it is difficult to conduct an electrical impulse (such an effect is called heart block in medical terminology).

- Violation of the formation of an electrical impulse — the reason is the presence of a competing impulse elsewhere, and a violation of the operation of the sinus node [13].

Arrhythmias caused by a violation of automaticity of the sinus node

- Sinus arrhythmia
- Sinus bradycardia
- Sinus tachycardia
- Atrial asystole
- Sinus node weakness syndrome
- Stopping the sinus node

Ectopic rhythms or complexes [14, 15]

2. Passive rhythms and complexes:

- Atrial.
- Migration of the supraventricular pacemaker.
- From the atrioventricular connection.
- Pop-up abbreviations.
- From the ventricles.

2. Active rhythms and complexes.

- Extrasystole:
- Gastric
- From the atrioventricular connection
- Atrial
- Parasystole
- Paroxysmal and non-paroxysmal tachycardia:
- Atrial form;
- From the atrioventricular junction;
- Gastric form.

Flickering and fluttering of the atria and ventricles

- Atrial flutter (fibrillation).
- Tremors and flickering of the ventricles.
- Atrial flutter.

Violations of the conductivity function

- Intraatrial blockade.
- Sinoatrial blockade.
- Violations of intraventricular conduction.
- Atrioventricular block.
- Syndromes of premature ventricular excitation: WPW syndrome, bundle branch blocks.
- Short P-Q interval syndrome.

Classification of arrhythmias according to clinical significance

- Benign arrhythmias (do not affect the prognosis of life).
- Potentially malignant arrhythmias (worse the prognosis of life).
- Malignant arrhythmias (life-threatening).

An ECG is a fairly informative and common study of the heart rhythm at rest. Some blockages and arrhythmias can be diagnosed during various tests with dosed physical activity. It is important to check the daily Holter monitoring, during

the day the heart rhythm is determined. It is possible to qualitatively and quantitatively characterize tachycardia and other arrhythmias, during physical exertion, and at rest to assess the effectiveness of treatment [16, 17].

Impulse generation disorder

Sinus arrhythmia

- Sinus bradycardia (less than 60 complexes in 1 min.)
- Sinus tachycardia (more than 90 complexes in 1 min.)
- Stopping of the sinus node
- Extrasystole (synonymous with premature depolarization)
- Migration of the supraventricular pacemaker.

Extrasystole

- Atrial
- Ventricular
- Atrioventricular (atrioventricular)

There can also be extrasystole

- Frequent (30 or more in 1 hour)
- Single (up to 30 in 1 hour)
- Polymorphic
- Alorhythmia (bigeminy, trigeminy, quadrigeminy)
- Early (R on T)
- Steamy

Tachycardia

- Supraventricular
- Atrial
- Sinoatrial
- Atrioventricular
- With additional ways of conducting: orthodromic; antidromic;
- Unstable (from 3 ventricular complexes to 30 per minute);

- Ventricular:
- Constant-inverse;
- Stand (more than 30s);
- Polymorphic;
- Monomorphic.

Fibrillation and flutter of the atria:

- Persistent (intervention is required to restore sinus rhythm)
- Paroxysmal (the rhythm is restored independently within 48 hours)
- Permanent (when it is impossible or impractical to restore sinus rhythm)
- Tachysystolic (frequency of ventricular contractions more than 90 in 1 minute)
- Bradysystolic (frequency of ventricular contractions less than 60 per 1 minute)
- Fibrillation and fluttering of the ventricles [18, 19].

Impulse conduction disorder.

1. Atrioventricular blockade (I–III degrees).
2. Sinoauricular blockades.
3. Intraventricular blockades (permanent, transient):

Single-beam blockades

- blockade of the right leg of the bundle of His;
- blockade of the anterosuperior branching of the left leg of the bundle of His;
- blockade of the posteroinferior branching of the left leg of the bundle of His;

Double beam blockades

- blockade of the left leg of the bundle of His;

- blockade of the right leg of His bundle and blockade of the posterior inferior branch of the left leg of His bundle (Wilson's blockade).
- blockade of the right leg of His bundle and blockade of the anterior superior branch of the left leg of His bundle (Bailey blockade).

Combined disorders of impulse formation and conduction

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Parasystole:

- atrial
- ventricular
- atrioventricular connection.

Diseases, syndromes and phenomena.

ECG phenomena and syndromes of premature ventricular excitation:

- the syndrome of shortening of the P-R interval (Laun-Ganong Levine or Clark-Levy-Kritesco);
- Wolff-Parkinson-White syndrome
- early ventricular repolarization syndrome
- sinus node weakness syndrome
- Frederick's syndrome
- Morganhi-Adams-Stokes syndrome
- syndrome of prolonged Q-T interval:
- acquired
- born (Romano-Warda) [20-24].

Sudden cardiac death (arrhythmic death) - death that occurred within 1 hour after the deterioration of the patient's condition, the appearance of the first symptoms of heart disease, or during the chronic course of the disease [25, 26]:

- irreversible
- with recovery of cardiac activity

Cardiac arrest (death occurring more than 1 hour after worsening of heart disease symptoms or onset of heart disease symptoms):

- irreversible
- with recovery of cardiac activity

Mechanisms of death:

- electromechanical dissociation
- asystole
- ventricular fibrillation

2.2. Arrhythmias with impaired function of pacemakers or with normal function of pacemakers of various types

Etiology

1. Nerve-reflex actions (in gastric ulcer, cholecystitis, diaphragmatic hernia, deforming osteochondrosis), electrolyte balance disorders (hyperkalemia, hypokalemia, hypercalcemia, hypomagnesemia), humoral regulation disorders, endocrine disorders, acid-base balance disorders [27, 28].

2. Diseases of the cardiovascular system: myocardial infarction, chronic ischemic heart disease, myocarditis, unstable angina, heart defects, cardiomyopathy, mitral valve prolapse.

3. Chemical and physical influences: alcohol, smoking, hypoxia, trauma, hyperthermia and hypothermia, medications (antiarrhythmics, cardiac glycosides, sympathomimetics, diuretics).

4. Arrhythmias are idiopathic.

Pathogenesis of cardiac arrhythmias

At the heart of arrhythmias is a violation of impulse conduction, impulse formation, or a violation of the functions of the heart's conduction system.

Sinus bradycardia and tachycardia are associated with suppression and enhancement of cell automatism in the sinus node.

In paroxysmal rhythm disturbances and extrasystole, the following mechanisms are distinguished:

- re-entry of excitation (re-entry), movement of the pulse in a circle
- strengthening of automaticity of ectopic foci
- trigger activity of contractile and specialized cells.

Mechanism of re-entry: multiple or repeated excitation of a limited number of cardiomyocytes by a single impulse that moves in a circle.

Two conduction paths are required, one path is disrupted due to a local unidirectional blockade.

The area of the myocardium, to which the next impulse did not reach, becomes a source of out-of-order excitation. It is excited with a certain delay due to the bypass. Excitement spreads to neighboring areas of the myocardium.

Complaints of the patient

Cardiac arrhythmias can be asymptomatic or with different clinical manifestations.

The main symptoms in a patient with a heart rhythm disorder:

- feeling of heartbeat
- a feeling of interruptions in the work of the heart.

Sinus tachycardia is accompanied by a feeling of increased heartbeat. Sinus tachycardia can occur with excitement, anxious thoughts, or excitement. Sinus tachycardia occurs during physical exertion [29].

Feelings of interruptions in the work of the heart often occur during extrasystole (extraordinary premature contraction of the heart). The patient complains of the feeling of the heart stopping for a short time, the heart stopping, a sudden strong shock in the area of the heart, dizziness, darkening of the eyes. Some patients say they feel their heart "turn over". They feel the need to take a deep breath.

With paroxysm of atrial fibrillation, the patient experiences an irregular heartbeat.

Arrhythmia can cause burning pain behind the sternum (angina), sudden general weakness, shortness of breath, dizziness, pulmonary edema, loss of consciousness, and cardiogenic shock [30-32].

Bradyarrhythmias and tachyarrhythmias are causes of loss of consciousness

Arrhythmias (ventricular fibrillation after ventricular tachycardia) are often the cause of sudden death.

Extrasystole

Premature excitation of the heart or premature excitation of parts of the heart under the influence of pathological impulses is called ecstasystole. There is a premature contraction of the heart followed by a long pause. The pause after extrasystole is called compensatory (postextrasystolic interval)

The complete compensatory pause is equal to the sum of the post-systolic interval and the extra-systolic interval of equal length of two cardiac cycles. If this amount is shorter, then such a compensatory pause is called incomplete.

Interpolated systole does not have a compensatory pause.

If extrasystole occurs regularly between normal cardiac complexes, it is called allorhythmic. If an extrasystole occurs after each normal complex, such an arrhythmia is called bigeminia. After two normal complexes, extrasystole occurs - tic arrhythmia is called trihymenia. Quadrigeminy is an arrhythmia with the appearance of an extrasystole after every three normal heart cycles. Extrasystoles can be group or single, paired (two extrasystoles in a row).

The time of occurrence of extrasystole is important. There are early and late extrasystoles. Early extrasystoles are superimposed on the T wave, middle extrasystoles have an interval with the T wave, and late extrasystoles appear in the second half of diastole. Early extrasystoles are more dangerous. They are ineffective in hemodynamics and can lead to the development of dangerous arrhythmias: ventricular fibrillation, atrial flutter or atrial fibrillation.

Also, extrasystoles can occur in different areas of the heart - polytopic extrasystoles, or originate from one area - monotopic. Polytopic extrasystoles indicate diffuse damage to the myocardium in different areas.

Atrial, ventricular and nodal extrasystoles are distinguished.

Atrial extrasystole

Atrial extrasystoles occur with atrial myocardium pathology. Group frequent atrial extrasystoles, polytopic atrial extrasystoles are predictors of atrial fibrillation, atrial flutter and atrial tachycardia [33].

A sign of atrial extrasystole is a premature different from the normal sinus wave R. The shape of the ventricular complex has not changed. Incomplete compensatory pause.

Ventricular complexes during atrial extrasystole are changed in violation of ventricular conduction. It can be a blockade of the right leg of the bundle of His.

There are also atrial extrasystoles with absent QRST. Such atrial extrasystole is called blocked [34].

Atrio-ventricular extrasystole (AV)

AVs are of different localization. There are high-nodal extrasystoles, low-nodal extrasystoles, and mid-nodal extrasystoles.

If the extrasystoles come from the AV node, then atrial excitation occurs first. Extrasystoles, they can arise from the lower parts of the atria - supraventricular extrasystoles.

If there are no P waves in the premature complexes (coinciding with the QRS on the graph), then these are AV extrasystoles with simultaneous excitation of the ventricles and atria.

If, after R waves, extrasystoles, negative R waves appear in leads II, III, and aVF, these are AV extrasystoles with atrial excitation at the end of the cycle.

After AV extrasystole, the compensatory pause can be incomplete or complete.

Ventricular extrasystole

If the focus of myocardial excitation is localized in the bundle of His, extrasystoles are ventricular [35, 36].

With such an arrhythmia, there is no P wave and a deformed QRS complex before the extrasystole. The duration of the QRS complex is more than >0.12 seconds. The ST segment and the T wave are discordant with respect to the QRS complex. Complete compensatory pause after ventricular extrasystole.

The shape of extrasystoles determines the location of the ectopic focus. Diagnosis is based mainly on chest leads.

When extrasystoles occur from the right ventricle, the complex is similar to the ECG graph when the left leg of the His trigger is blocked.

Extrasystoles from the left ventricle are similar to complexes with blockade of the left leg of the bundle of His.

If the QRS complexes in all chest leads are directed upward and expanded, these are basal extrasystoles.

If the S wave amplitude is the largest on the ECG graph, these are apical extrasystoles (apical extrasystoles) [37].

Classification of extrasystoles according to V. Lown

The classification is based on the frequency of occurrence, prognosis of tachyarrhythmia development and foci of extrasystoles (Fig. 1).

Class I - rarely occurs, monotopic, up to 5 in 1 minute. or 30 for 1 hour

Class II - frequent monotopic, >5 in 1 minute. or >30 in 1 hour

Class III – polytopic extrasystoles

Class IV – paired extrasystoles (two contractions in a row)

Class IV – three (or more) extrasystoles in a row (short paroxysms)

Class V – "early" extrasystoles (R on T)

Figure 1. Classification of extrasystoles.

Paroxysmal tachycardia

Paroxysmal tachycardia is a sudden increase in heart rate [38, 39].

Signs of paroxysmal tachycardia:

1) heart rate 160–250 beats per minute.

2) correct sinus rhythm,

3) heterotopicity

Sometimes the heart rate is 130–150 per minute. But the rhythm is irregular sinus.

Attacks of paroxysmal tachycardia begin suddenly and end suddenly.

Attacks of paroxysmal tachycardia can last several days, weeks, months) or be short, for example 5 or more complexes.

Paroxysmal tachycardia can originate from the atria and ventricles: supraventricular paroxysmal tachycardia and ventricular paroxysmal tachycardia.

Supraventricular paroxysmal tachycardia

With supraventricular paroxysmal tachycardia, the ventricular complexes are not deformed.

Supraventricular paroxysmal tachycardia can originate from the atria or from the atrio-ventricular node.

Atrial paroxysmal tachycardia

There is a changed P wave before the ventricular complex and a shortening or lengthening of the PQ interval.

Atrio-ventricular paroxysmal tachycardia

Atrio-ventricular paroxysmal tachycardia is characterized on the ECG by the location of the negative P wave after the QRS complex in leads II, III, aVF.

Atrio-ventricular paroxysmal tachycardia is often resistant to pharmacotherapy and vagal tests [40].

Paroxysmal ventricular tachycardia

The frequency of the rhythm is from 130 to 270 per minute, more often 160-220 per minute. Extended and deformed QRS complex, duration more than 0.13 seconds. The ST interval and the T wave are discordant with respect to the R or S wave, similar to ventricular extrasystole.

Sometimes P waves are autonomous, not associated with the QRS complex.

During the period without a paroxysm, the patient has ventricular extrasystoles similar to the complexes of the period of paroxysmal ventricular tachycardia, that is, they originate from one ectopic focus of excitation.

The localization of the focus of excitation in ventricular tachycardia is determined by the chest leads of the ECG.

Paroxysms of ventricular tachycardia occur in patients with severe heart disease, often with acute myocardial infarction, and can lead to the development of ventricular fibrillation or ventricular flutter and require immediate treatment.

Atrial fibrillation

Atrial fibrillation and atrial flutter are arrhythmias classified as atrial fibrillation.

Atrial fibrillation (atrial fibrillation) is a frequent, chaotic irregular excitation and contraction of individual groups of cardiomyocytes in the atria. The frequency of contraction of muscle groups in the atria is from 370 to 700 per 1 minute. Most impulses are received in the atrio-ventricular node and do not enter the ventricles. Those impulses that pass to the ventricles cause them to contract irregularly.

There are no P waves on the ECG. There are f waves, different in graphics, with different frequency. F waves are clearly visible in ECG leads II, III, and VF and V1.

Waves f can be different in amplitude. Large-wave and small-wave atrial fibrillation are distinguished depending on the amplitude of the f waves. R-R intervals have different lengths.

Classification of atrial fibrillation according to the frequency of ventricular contractions:

- tachysystolic with a ventricular rate greater than 60 per 1 minute
- normosytolic with a ventricular rate of 60–90 per minute
- bradysystolic with a ventricular rate of less than 60 per 1 minute

Atrial fibrillation can be permanent (persistent), paroxysmal or persistent.

At a very high frequency of the atrial rhythm, 250-370 per minute, the atrial fibrillation is called atrial flutter.

On the ECG: rhythmic F waves that look like saw teeth. F waves have a constant shape in each of the leads on the ECG. The F waves are wide and there is no interval. F waves are better visible in leads II, III, aVF and V1-2.

Rhythmic ventricular contractions occur after every arch, third, fourth or other regular atrial wave. With such an arrhythmia, atrial flutter occurs with the correct conduction of impulses to the ventricles and the ratios are indicated: 2:1, 3:1, 4:1.

With an irregular ventricular rhythm, atrial flutter is called irregular, similar to atrial fibrillation by clinical signs.

There are stable, persistent, paroxysmal, permanent forms of atrial flutter.

Atrial flutter is less common than atrial fibrillation. Atrial flutter can pass and flicker and vice versa [41].

When complete atrio-ventricular block and atrial fibrillation are combined, Frederick's syndrome occurs [42].

Fluttering and fibrillation of the ventricles

With ventricular fibrillation and ventricular flutter, the patient's blood circulation stops. These arrhythmias are the cause of death (arrhythmic death).

Ventricular fibrillation - irregular uncoordinated, chaotic contractions of the cardiomyocytes of the ventricles with a frequency of 200-500 per minute. On the ECG, irregular waves of different amplitudes, different lengths between waves. Ventricular fibrillation can be short-wave or short-wave. The amplitude of waves

in large-wave ventricular fibrillation is more than 0.5 mV. In the case of short-wave radiation - less than 0.5 mV.

Ventricular flutter is a rhythmic contraction of the ventricles with a frequency of 200-300 per minute. On the ECG, the curve is similar to the teeth of a saw, the wave shape and amplitude are the same, but you cannot see individual complexes of the heart rhythm, there are no intervals.

2.3. **Treatment of arrhythmias**

Classification of antiarrhythmic drugs

There are 4 classes of antiarrhythmic drugs (Fig. 2).

Class I - blockers of fast sodium channels

Class IA - quinidine, novocainamide, hylurithmal disopyramide

Class IB - lidocaine, trimecaine, mexiletine, difenin

Class IC - etacizin, etmosin, propafenone (Rytmonorm), flecainide, alapinin

Class II - β - adrenoblockers

Class III - increase the action potential and slow down repolarization, blockers of potassium channels - amiodarone (cordarone), bretylium, sotalol

Class IV - blockers of slow calcium channels - verapamil, diltiazem

Figure 2. Classification of antiarrhythmic drugs.

Alanidine is a specific bradycardic drug.

Adenosine - stimulates purinergic receptors of cardiomyocytes.

Propafenone has a class IC effect and is a calcium antagonist and β-adrenoblocker.

Treatment of extrasystolic arrhythmia

Treatment depends on the prognosis of the arrhythmia for the patient and clinical manifestations.

It is necessary to take into account:

- the condition of the structural parts of the heart, there is a risk of dangerous arrhythmias.

- patient complaints.

Medicines are prescribed for extrasystolic arrhythmia in the following cases:

- Progressive heart disease and a significant increase in the number of extrasystoles.

- Extrasystoles are group, paired, polytopic, frequent, early ventricular (R on T) and threaten the patient's life.

- Bigeminy, trigeminy, quadrigeminy, allorhythmia, paroxysms of atrial tachycardia in heart failure.

- Extrasystoles in patients with mitral valve prolapse or with prolonged Q-T interval syndrome, which are arrhythmogenic effects.

- During angina attacks or during the development of an acute myocardial infarction, the number of extrasystoles increases.

- Paroxysm of ventricular tachycardia or ventricular fibrillation with subsequent ventricular extrasystoles.

- Abnormal pathways of conduction of electrical impulses (CC syndrome and WPW syndrome) with extrasystolic arrhythmia.

If the patient's extrasystoles are not life-threatening and the patient has no complaints, pharmacotherapy is not required. Extrasystoles in young people in the absence of structural abnormalities do not require pharmacological treatment either [43].

With poor tolerance of extrasystolic arrhythmia, in such cases, the patient is prescribed sedative drugs, antidepressants or tranquilizers. Patients with chronic diseases of internal organs (gastric ulcer disease, cholecystitis) with extrasystolic arrhythmia are treated for the underlying disease and psychotropic drugs may be

used. If the functions of the autonomic nervous system are impaired, M-cholinergics or β-adrenergic blockers are used [44].

Treatment of supraventricular extrasystole with existing complaints is carried out by calcium antagonists (diltiazem or verapamil). Second-line drugs are β-blockers. If there is no effect from the treatment, class I antiarrhythmic drugs or combined antiarrhythmic therapy are prescribed.

Patients who have refractory arrhythmia or threatening conditions with impaired hemodynamics, paroxysms of ventricular tachycardia, coronary blood flow disorders, paroxysms of ventricular fibrillation are treated surgically. Surgical treatment includes implantation of special devices, destruction of foci of ectopic rhythm or other interventions.

Treatment of supraventricular paroxysmal tachycardia

Treatment of supraventricular paroxysmal tachycardia includes reflex stimulation of the vagus nerve. The following samples are used [45, 46]:

1. Valsalva trial . The patient is asked to hold the breath (Fig. 3).

Figure 3. Valsava test.

2. Chermak-Goering test. A massage is carried out in the area of the corytid sinus (Fig. 4).

Figure 4. Chermak-Goering test.

3. Aschner-Dunny test. The patient himself or another person presses the thumbs on the eyeballs with closed eyes below the browbones (Fig. 5).

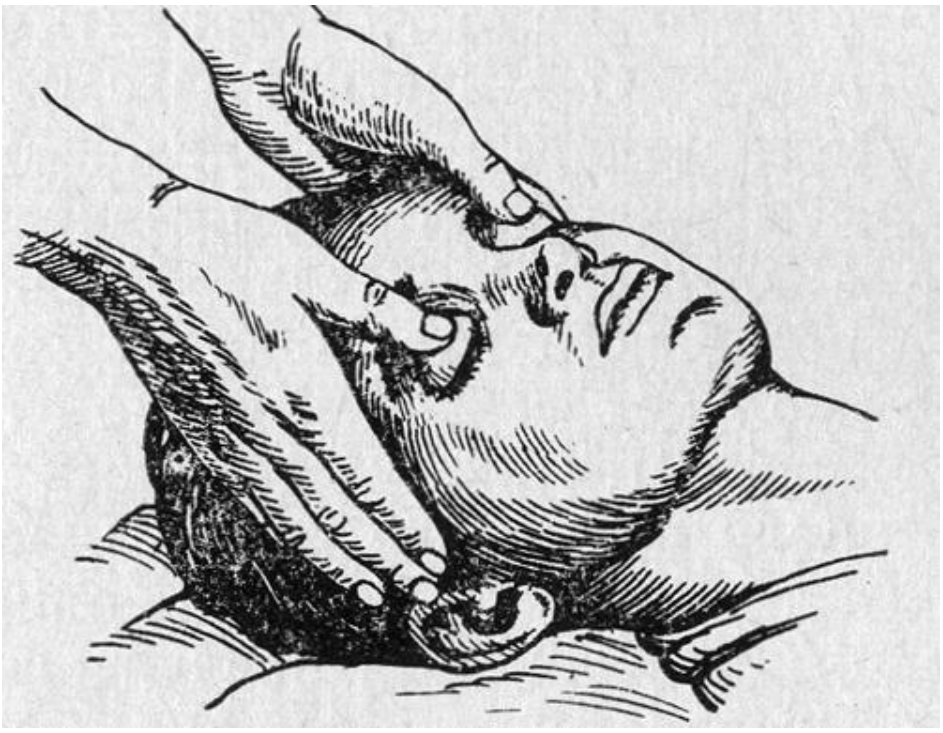

Figure 5. Aschner-Dunny test.

4. Reproduction of the vomiting reflex (Fig. 6).

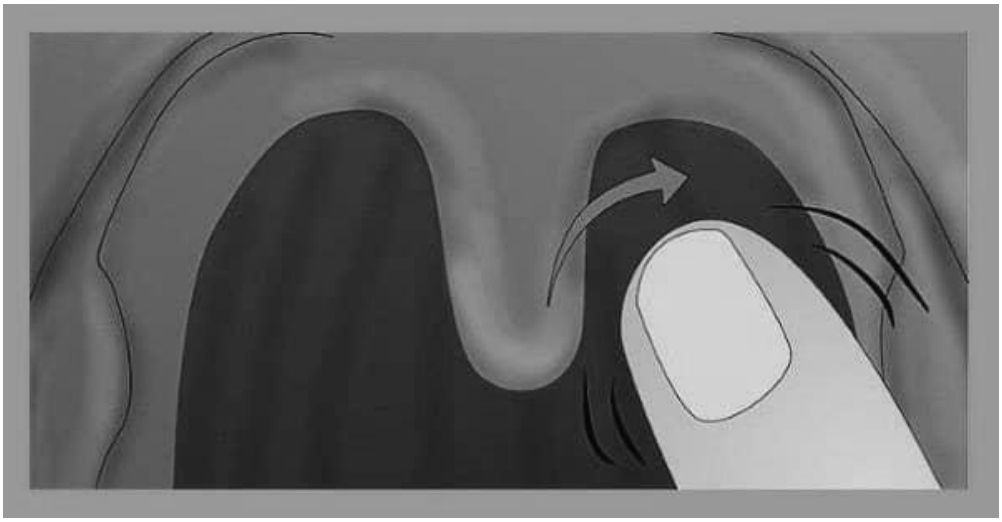

Figure 6. Vomiting reflex (test).

4. "Diving reflex" - immersing the face in cold water with a breath hold (Fig. 7).

Figure 7. Diver's reflex

5. Balloon inflation test (Fig. 8).

Figure 8. Balloon inflation test.

2.4. Pharmacotherapy

First-line drugs are verapamil and adenosine triphosphate [47, 48].

Verapamil 5 mg or 10 mg intravenously 2 ml of 2.5% solution in 5 minutes or 4 ml in 10 minutes. You can repeat the dose if there is no effect.

Adenosine triphosphate intravenously 1–2 ml of a 1% solution to be administered in 5–10 seconds. It can be repeated in the same dose if there is no effect.

Propafenone 150 mg IV for 10 min. Further introduction slowly into a vein in 2 hours.

Amiodarone i/v jet 5% solution 6 ml for 2–3 min.. Further administration drip in 250 ml of 5% glucose solution 6 ml for 1–2 hours.

Obsidan - 5 ml of 0.1% solution in 0.9% NaCl 10 ml.

Potassium preparations increase the effectiveness of antiarrhythmic drugs.

If medical therapy is ineffective, electrical cardioversion is performed.

Indications for electrical cardioversion [49]:

- arrhythmic collapse

- acute left ventricular failure
- myocardial infarction
- unstable angina pectoris
- acute coronary insufficiency during an attack of paroxysmal tachycardia.

Transesophageal electrocardiostimulation is performed at:
- ineffectiveness of pharmacotherapy
- Contraindications for pharmacotherapy
- Violation of hemodynamics
- Paroxysm of supraventricular tachycardia with the arrhythmogenic effect of antiarrhythmic drugs.

Implantation of an antitachycardial pacemaker is indicated for
- patients with supraventricular paroxysmal tachycardia with significantly worsened general condition
- patients with arrhythmia recurrences during pharmacological treatment
- refractory patients to antiarrhythmic drug therapy [50].

2.5. Surgical treatment

Surgical treatment is indicated for patients:
- with tachycardia with a frequency of ventricular contractions of more than 200 per minute.
- Young age
- With a violation of hemodynamics during a paroxysm of tachycardia
- During pregnancy
- With ineffective pharmacotherapy
- In case of drug intolerance
- With atrial fibrillation and additional conduction pathways
- With a disability.

The focus of ectopic excitation is surgically removed or this focus is fixed or isolated.

Prevention of arrhythmia

Used to prevent arrhythmia:

- long-acting verapamil 240 mg per day
- sotalol 3–5 mg/kg/day
- cordarone 200 mg per day with intermittent intake (5 days of taking and 2 days off)
- Obzidan 240 mg per day.

Treatment of ventricular tachycardia

In the event of ventricular tachycardia with hemodynamic disturbances, ventricular cardiostimulation or electrical cardioversion should be performed immediately [51].

In case of ventricular tachycardia without hemodynamic changes, perform a precardial stroke (Fig. 9).

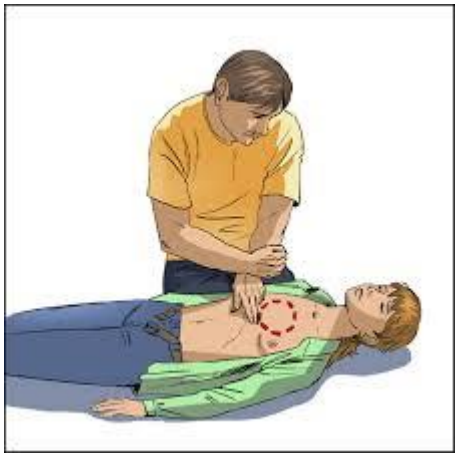

Figure 9. Precardiac stroke.

After a precardial stroke, drug therapy is used:

- Novocainamide 10 ml of 10% solution. Efficiency 70%.
- Amiodarone. The initial dose is 300–450 mg.
- Lidocaine 80–120 mg

When the patient's condition is stabilized, supportive antiarrhythmic therapy is used:

- Amiodarone
- class I antiarrhythmic drugs

Electrical cardioversion is performed at:

- ineffectiveness of drug therapy;
- clinical manifestations from the onset of paroxysmal tachycardia (collapse, acute left ventricular failure, acute coronary insufficiency).

Electrocardiostimulation (transesophageal, endocardial) is indicated when electrical cardioversion and drug therapy are ineffective.

Surgical treatment of patients with ventricular tachycardia includes the following methods:

- Aneurysmectomy
- Radiofrequency ablation
- Installation of a cardioverter (defibrillator)
- Heart transplant.

Treatment of atrial fibrillation

Stopping a paroxysm of atrial fibrillation [52].

If an attack with hemodynamic disorders with the development of fainting, collapse, cardiac asthma, pulmonary edema, angina pectoris, electrical cardioversion is indicated. If the paroxysm of atrial fibrillation lasts up to 48 hours, it is recommended to introduce unfractionated heparin 4000–5000 IU or low molecular weight heparins.

If the paroxysm lasts more than 48 hours, it is recommended to prepare the patient using warfarin before restoring the rhythm.

The first episode of administration of an antiarrhythmic drug should be carried out under the control of ECG monitoring.

Atrial fibrillation lasting up to 7 days is recommended to use:

- Amiodarone
- Propafenone
- Quinidine
- Novocainamide.

Atrial fibrillation lasting more than 7 days is recommended to use:

- Amiodarone
- Propafenone
- Quinidine
- Novocainamide.

It is contraindicated to use sotalol and cardiac glycosides

Cardioversion with propafenone:

Propafenone 150 mg intravenously for 10 minutes, then drip-75 mg for 2 hours.

Amiodarone cardioversion:

Amiodarone 300 mg in 250 ml of 5% glucose solution for 1 hour IV, then 900 mg in 500 ml of 5% glucose solution for 23 hours.

Cardioversion with novocaine

Novocainamide 10 ml of 10% solution in 10 ml of isotonic NaCl solution intravenously for 8–10 min. under constant control of heart rate, blood pressure, and ECG.

Prevention of paroxysm of atrial fibrillation:

propafenone 0.15

quinidine 0.2 1 t.

amiodarone 1 t per day

sotalol 0.08–0.32

If frequent paroxysms persist, antiarrhythmic drugs are ineffective, radiofrequency ablation is recommended.

In the absence of an effect from radiofrequency catheter ablation, it is recommended to use drugs to slow down the heart rate: digoxin with a β-blocker in combination with anticoagulants.

Treatment of permanent and persistent form of atrial fibrillation.

1. heart rate control: normalization of heart rate while maintaining atrial fibrillation requires the use of anticoagulants.

2. rhythm control: restoration of sinus rhythm and prevention of relapses.

With safe cardioversion, sinus rhythm should be restored and sinus rhythm should be maintained. The indication is the young age of the patient, the average age of the patient, the first episode of atrial fibrillation, clinically significant arrhythmia.

Heart rate monitoring is chosen for patients older than 65 years with a complicated medical history:

- transient ischemic attack,
- ischemic stroke,
- valvular heart disease,
- thromboembolism,
- dimensions of the left atrium >5.5–6 cm,
- structural disorders of the left ventricle (postinfarction cardiosclerosis, cardiomegaly, chronic heart aneurysm, ejection fraction <40%),
- thrombus in the left atrium,
- thyrotoxicosis,
- active rheumatism,
- myocarditis,
- sinus node weakness syndrome,
- severe obesity,

- the duration of the episode is more than 3 years.

Before performing cardioversion, use warfarin until the MNS is 2.0–3.0 within 3–4 weeks, amiodarone 0.6–0.8 per day.

After restoring the rhythm, the patient should take warfarin for 4 weeks.

The effectiveness of electrical cardioversion in atrial fibrillation is 90-96%. Potassium preparations, verapamil or β-blockers, digoxin are prescribed for 10 days. Digoxin is canceled in 4 days, verapamil or β-blockers are canceled a day before electrical cardioversion.

Heart rate control in chronic form of AF.

diltiazem 120 mg or 240 mg;

digoxin 0.125–0.25 per day;

β - blockers.

verapamil 120 or 240 mg per day;

Additionally:

amiodarone 100–300 mg per day.

sotalol 40–160 mg per day;

A combination of cardiac glycosides with Ca antagonists or β-blockers is optimal.

Non-pharmacological treatment of atrial fibrillation [53]:

internal atrial defibrillators

atrial stimulation

catheter ablation

surgical ablation

Treatment of atrial flutter

- Radiofrequency catheter ablation of the cava-tricuspid isthmus is effective in 95% of cases.

- cessation of atrial flutter after transesophageal stimulation of the heart in 67% of cases leads to restoration of sinus rhythm and in 33% of cases leads to atrial fibrillation.

- electropulse therapy with a power of 100–200 J

- Class I antiarrhythmic drugs are highly likely to slow down the wave frequency and cause 1:1 conduction.

- Prescribe anticoagulant therapy [54].

If it is impossible to restore sinus rhythm, patients with a permanent form of atrial flutter are recommended to be transferred to atrial flutter. Atrial flutter is easier to control with amiodarone, digoxin, sotalol in relation to the frequency of contractions.

Reasons for the development of arrhythmia [55]:

- the presence of heart diseases
- hereditary predisposition
- thyroid disease
- stress (arrhythmia in neurotic conditions)
- alcohol abuse
- arterial hypertension
- pathology of the stomach, intestines or gall bladder, flatulence (arrhythmia after eating)
- use of certain medications (decongestants).

Symptoms of arrhythmia

1. Feeling of tachycardia or bradycardia
2. Chest pains
3. Dizziness
4. Shortness of breath
5. Loss of consciousness.

Some types of arrhythmia can be without clinical signs in the patient.

2.6. Macrolides

Macrolides are a group of antimicrobial agents of natural and semi-synthetic origin. Macroliths are able to penetrate inside cells. In the environment of cells, macrolides affect intracellular pathogens: chlamydia, mycoplasma, legionella, campylobacter.

The basis of the chemical structure of macrolides is the macrocyclic lactone ring. One or more carbohydrate residues are attached to the ring.

Classification of macrolides

Classification of macrolides by chemical structure (14-, 15-, and 16-membered ring), method of preparation, and duration of action [56].

Natural macrolides include oleandomycin and erythromycin (14-membered lactone ring) and midecamycin, josamycin, and spiramycin (16-membered lactone ring). Semi-synthetic macrolides are clarithromycin, flurithromycin, roxithromycin, dirithromycin, and telithromycin (14-membered lactone ring); azithromycin (15-membered lactone ring); rokitamycin and myocamycin (16-membered lactone ring).

Short-acting macrolides include erythromycin and midekamycin. spiramycin, rokitamycin and oleandomycin. Clarithromycin, josamycin, flurithromycin and roxitroycin have a medium-term effect. Azithromycin and dirithromycin are long-acting macrolides.

Macrolides create a high concentration in average cells, the concentration of macrolides in blood plasma is much lower than in tissues. Macrolides penetrate into breast milk and through the placenta. Through the hemato-ophthalmic and hematoencephalic barriers penetrate poorly. Metabolism occurs in the liver in phase I and metabolites are excreted with bile.

Macrolides disrupt protein synthesis at the stage of translation in bacterial cells due to reversible binding to the 50S subunit at any stage of the ribosomal

cycle. The peptidyl-tRNA peptide chain is disconnected and the formation of the polypeptide is stopped [57].

Therapeutic concentrations of macrolides have a bacteriostatic effect, high concentrations have a bactericidal effect. They also have an anti-inflammatory effect and an immunomodulatory effect. Macrolides accumulate in active neutrophils and migrate to foci of inflammation. Macrolides increase anti-inflammatory cytokines, decrease pro-inflammatory cytokines and free radical oxidation, activate phagocytosis and chemotaxis, reduce mucus secretion, and improve mucocidal clearance [58].

Macrolides act on pneumococcus, the causative agent of diphtheria and pertussis, β-hemolytic streptococcus group A. Macrolides are used to treat upper respiratory tract infections, soft tissue and skin infections, community-acquired pneumonia, urogenital infections, intestinal campylobacteriosis, venereal diseases, and in the Helicobacter eradication scheme pylori.

The risk of developing side effects is more common when using erythromycin.

Main side effects:

- phlebitis and thrombophlebitis with intravenous administration
- headache, dizziness
- fever, jaundice, weakness, nausea, abdominal pain, vomiting
- reverse ototoxicity
- paresthesias, asthenia, increased excitability, insomnia, nervousness
- impaired perception of smell and taste
- transient increase in the activity of transaminases
- cholestatic hepatitis
- decrease in blood pressure
- arrhythmia
- increase in the Q–T interval.

CHAPTER 2

Materials and methods of research

2.1. Clinical characteristics of examined patients with heart rhythm disorder

We analyzed 30 stories of patients with heart rhythm disorder. Of these, 17 (57%) female patients and 13 (43%) males (Fig. 1).

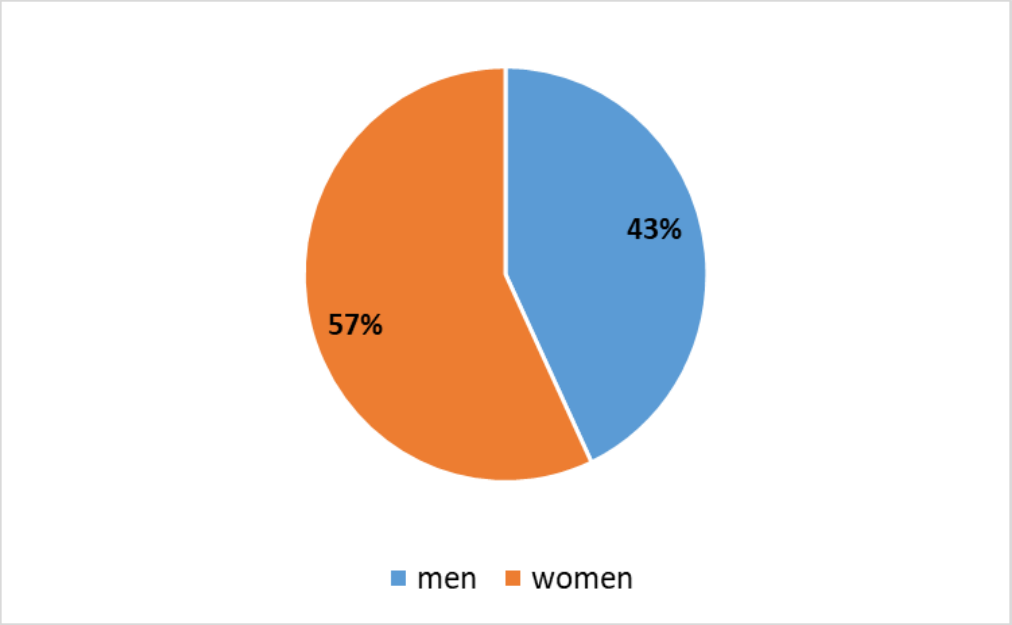

Figure 2.1. Distribution of patients by sex.

The average age of the examined patients was 55.3±3.7 years. The duration of the disease was an average of 3.8 ± 1.2 years.

All patients had different types of arrhythmia. 15 patients with sinus arrhythmia (I group), 9 patients with atrial arrhythmia (II group) and 6 patients with extrasystolic arrhythmia (III group) (Fig. 2).

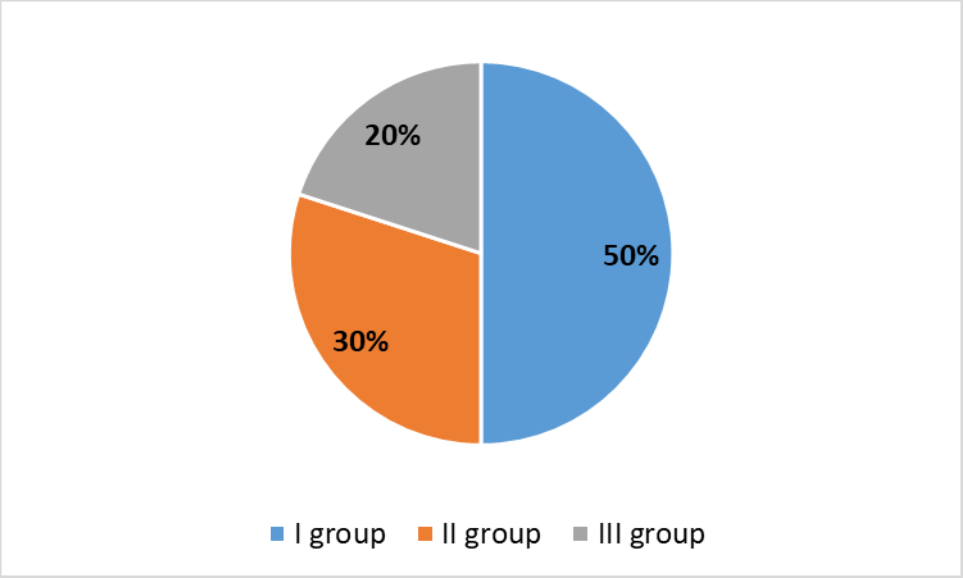

Figure 2.2. Distribution of patients by type of cardiac arrhythmia

All patients received drug treatment with more than 1 drug. Among the macrolides, azithromycin and spiromycin were prescribed.

CHAPTER 3
RESULTS OF OWN RESEARCH

3.1. The frequency of concomitant pathology in patients with heart rhythm disorders who took macrolides

When analyzing 30 disease histories of patients with heart rhythm disorders, it was found that all patients had concomitant diseases (Table 3.1).

Table 3.1.

Analysis of concomitant pathology in patients with atrial fibrillation who took macrolides.

Disease	n	%
AH	11	37
BA	2	7
Type 2 diabetes	4	13
Arthrosis	6	20
Gastritis	8	27
Pneumonia	27	90
Soft tissue infection	2	7
Chlamydia trachomatis	1	3

11 patients (37%) had a concomitant disease of arterial hypertension (AH), 2 (7%) patients had bronchial asthma (BA), 4 patients (13%) had type 2 diabetes, 6 patients (20%) had joint diseases , 8 patients (27%) suffered from gastritis.

27 patients (90%) received macrolides for the treatment of pneumonia, 2 patients (7%) received macrolides for the treatment of soft tissue infection, and 1 patient (3%) was treated with a macrolide for chlamydia.

3.4. Analysis of risks of complications in patients with cardiac arrhythmias who took macrolides.

Among the contraindications for the use of macrolides are the syndrome of prolonged QT interval, arrhythmias, bradycardia, severe violations of liver and kidney function.

Macrolide antibiotics are contraindicated for coagulation in patients with prolonged QT syndrome (acquired or congenital, with QT>0.44). An ECG analysis was performed and the duration of the QT interval was determined (Table 3.2).

Table 3.2.

The value of the QT interval in patients of different groups

Patient`s groups	QT (мм)
I	0.39±0.03
II	0.40±0.03*
III	0.36±0.02

Note: * - In patients with atrial fibrillation, the QT interval was determined when sinus rhythm was restored.

In patients with sinus arrhythmia, the average value of the QT interval was 0.39±0.03 mm, in patients with atrial fibrillation - QT 0.40±0.03 mm, and in patients with extrasystolic arrhythmia - QT 0.36±0.02 mm .

An analysis of heart rate (HR) was carried out (Table 3.3)

Table 3.3.

Heart rate in patients of different groups

Patient`s groups	Heart rate (bpm)
I	74,2±5,4
II	72,8±12,8*
III	84,2±3,7

Note: * - In patients with atrial fibrillation, the frequency of ventricular contractions was determined.

On average, heart rate in patients of group I was 74.2±5.4 beats/min, in patients of group II - 72.8±12.8 beats/min, and in patients of group III - 84.2±3.7 beats/min .

2 patients of the 1st group had a heart rate of less than 65 bpm.

The functional state of the liver and kidneys was also analyzed according to laboratory indicators (Table 3.4).

Table 3.4.

Laboratory indicators of the state of the liver and kidneys in patients with cardiac arrhythmias who took macrolides.

Indexes	Groups		
	I	II	III
ALT (U/L)	32,3±12,4	39,3±2,8	34,3±10,1
AST (U/L)	31,5±8,2	38,5±1,2	36,5±7,3
Creatinine (μmol/l)	101,3±4,2	112,3±8,3	68,3±1,2

On average, transaminases in patients of all groups were within the reference values. In patients of group I, ALT was on average 32.3±12.4 units/l, in patients of group II - 39.3±2.8 units/l, and in patients of group III 34.3±10.1 units/l. AST, respectively, 31.5±8.2 U/l, 38.5±1.2 U/l and 36.5±7.3 U/l.

Although transaminase levels were on average normal in patients of all groups, elevated ALT levels were found in 4 patients (13%) with arrhythmia who received macrolides (3 patients in group II and 1 patient in group III).

Based on the results of examinations, renal dysfunction was assessed by the level of creatinine. So, the average value of creatinine in patients of group I was 101.3±4.2 μmol/l, in patients of group II - 112.3±8.3 μmol/l, and in patients of group III - 68.3±1.2 μmol / l.

Among the patients of the II group, two patients had a creatinine level higher than 115 μmol/l, which is higher than the norm.

Therefore, among the patients with arrhythmias treated with macrolides, there were 2 patients (6%) with bradycardia, 4 patients (12%) with impaired liver function, and 2 patients (6%) with impaired renal function, which increases the risk of complications during treatment.

3.5. Analysis of the treatment of patients with cardiac arrhythmias who took macrolides.

In addition to the functional state of the liver, kidneys, and heart, complications during treatment with macrolides can occur due to irrational drug interactions.

We conducted an analysis of the treatment of patients with arrhythmias who took macrolides.

Group I patients were treated with antihypertensive, hypoglycemic drugs, and glucocorticoids.

Beta-blockers (bisoprol) were taken by 7 patients (23%), calcium channel blockers (amlodipine) were taken by 3 patients (10%), diuretics (hydrochlorothiazide, indapamide) were taken by 4 patients (13%), 1 patient took moxogam, 4 patients (13%) – ACE inhibitors (anelapril) and 2 patients (7%) took glucocorticoids (dexamethasone) (Table 3.5).

Table 3.5.

Intermedical interaction of patients of the I group

Drugs	Bisoprolol	Amlodipine	Indapamide	Hydrochlorothiazide	Moxonidin	Dexamethasone	Metformin
Azithromycin Spiramycin	-	metabolism of Azithromycine ↓	QT prolongation	QT prolongation	-	concentration of Dexamethasone ↑	-

Bisoprolol, Moxonidin, metformin with macrolides - there are no drug interactions.

Amlodipine with macrolides: the metabolism of macrolides can be decreased

Indapamide, Hydrochlorothiazide with macrolides: the risk or severity of QT prolongation

Dexamethasone with macrolides: The serum concentration of Dexamethasone can be increased [60-62].

The analysis of inter-medical interactions of patients of the II group is shown in table 3.6.

Table 3.6.

Intermedical interaction of patients of the II group

Drugs	Bisoprolol Pregabalin Furosemide Nitrosorbide Pantoprazole	Amiodarone	Warfarin
Azithromycin Spiramycin	-	Metabolism of Azithromycin ↓	Adverse effects

In the II group, bisoprolol (3 patients), pantoprazole (2 patients), pregabalin (2 patients), furosemide (3 patients), nitrosorbide (1 patient), clopidogrel (2 patients), amiodarone (3 patients) and warfarin (2 patients) were taken.

Bisoprolol, pregabalin, furosemide, nitrosorbide, clopidogrel, pantoprazole with macrolides - there are no drug interactions.

Amiodarone with macrolides: The metabolism of Azithromycin can be decreased

In group III, 2 patients took a local antacid, 1 patient took levofloxacin, and 3 patients took pantoprazole (table 3.7)

Table 3.7.

Intermedical interaction of patients of the III group

Drugs	Pantoprazole	Levofloxacin	Aluminum hydroxide/ magnesium hydroxide
Azithromycin Spiramycin	-	QT prolongation	-

Pantoprazole, Aluminum hydroxide/magnesium hydroxide with macrolides - there are no drug interactions.

Levofloxacin with macrolides: risk of QT prolongation

CONCLUSIONS

1. Risks of treatment complications due to bradycardia (7% of cases), impaired liver function (13% of patients) and impaired kidney function (7% of cases) were identified in patients with heart rhythm disturbances when using macrolides.

2. Among the undesirable drug interactions in patients with cardiac arrhythmias when using macrolides in 30% of cases is a change in the metabolism of the antibiotic, and QT prolongation in 17% of patients and slowing down the metabolism of another drug with the risk of developing side effects in 10% of patients.

PRACTICAL RECOMMENDATION

In patients with cardiac arrhythmias, when choosing a macrolide antibiotic, the risk of developing dangerous arrhythmias (prolongation of the QT interval) should be analyzed and, if possible, antibiotics of other groups should be used.

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62. FDA Approved Drug Products: Celestone Soluspan (betamethasone sodium phosphate and betamethasone acetate) injectable suspension

SUMMARY

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RISK MANAGEMENT OF MACROLIDE USE IN PATIENTS WITH CARDIAC ARRHYTHMIA

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Keywords: Cardiac arrhythmias, macrolides, treatment risks.

Introduction. Actuality of theme.

Violation of the heart rhythm is a violation of the conduction or occurrence of an electrical impulse in the heart muscle. Arrhythmias can occur with pathology of the sinoatrial node, with organic damage to the myocardium, with somatic diseases of other organs. The impetus for the development of arrhythmia can even be the influence of external factors. Patients of any age may be at risk of developing acute bacterial infection of the soft tissues, respiratory system, genitourinary tract, muscles, and skin, requiring antibacterial therapy. Antibiotics of different groups are used to select adequate antibiotic therapy, some of them show cardiotoxicity. In recent years, allergic reactions to antibacterial drugs from the group of penicillins and cephalosporins often occur, which causes the doctor to choose a drug from the group of macrols.

Materials and methods. An analyzed 30 stories of patients with heart rhythm disorder (57% female patients and 43% males). The average age of the examined patients was 55.3±3.7 years. The duration of the disease was an average of 3.8 ± 1.2 years. Among the macrolides, azithromycin and spiromycin were prescribed.

Results. 27 patients (90%) received macrolides for the treatment of pneumonia, 2 patients (7%) received macrolides for the treatment of soft tissue infection, and 1 patient (3%) was treated with a macrolide for chlamydia.

Among the patients with arrhythmias treated with macrolides, there were 2 patients (6%) with bradycardia, 4 patients (12%) with impaired liver function, and

2 patients (6%) with impaired renal function, which increases the risk of complications during treatment.

Amlodipine with macrolides: the metabolism of macrolides can be decreased. Indapamide, Hydrochlorothiazide with macrolides: the risk or severity of QT prolongation. Dexamethasone with macrolides: The serum concentration of Dexamethasone can be increased. Amiodarone with macrolides: The metabolism of Azithromycin can be decreased. Levofloxacin with macrolides: risk of QT prolongation.

Conclusions. Risks of treatment complications due to bradycardia (7% of cases), impaired liver function (13% of patients) and impaired kidney function (7% of cases) were identified in patients with heart rhythm disturbances when using macrolides. Among the undesirable drug interactions in patients with cardiac arrhythmias when using macrolides in 30% of cases is a change in the metabolism of the antibiotic, and QT prolongation in 17% of patients and slowing down the metabolism of another drug with the risk of developing side effects in 10% of patients.