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Название публикации: «TREATMENT AND PREVENTION VENTRICULAR ARRHYTHMIAS AFTER MYOCARDIAL INFARCTION, AND IN TYPE 2 DIABETIC MELLITUS PATIENTS WHO RECENTLY UNDERGONE MYOCARDIAL INFARCTION»

KALIT SO'ZLAR
Yurak ishemik kasalligi, Aritmiya, Koronar arteriya kasalligi, O'tkir miokard infarkti, To'satdan yurak o'limi, Qorinchalar taxikardiyasi, ST segmenti ko'tarilishi miokard infarkti, Revaskulyarizatsiya, Akseleratsiyalangan qorinchalar taxikardiyasi.

КЛЮЧЕВЫЕ СЛОВА
Ишемическая болезнь сердца, Аритмия, Ишемическая болезнь сердца, Острый инфаркт миокарда, Внезапная сердечная смерть, Желудочковая тахикардия, инфаркт миокарда с подъемом сегмента ST, Реваскуляризация, Ускоренная желудочковая тахикарди

KEY WORDS
Ischemic heart disease, Arrhythmia, Coronary artery disease, Acute miacardial infarction, Sudden cardiac death, Ventricular tachycardia, ST segment elevation myocardial infarction, Revascularization, Accelarated ventricular tachycardia.

ANNOTATION

Юрак ва кон-томир касалликлари бутун дунеда шу жумладан Узбекистонда хам кенг таркалган. Республикамиз ахолиси орасида ногиронликка ва улимга олиб келувчи сабаблар орасида юрак ишемик касаллиги ва аритмиялар етакчи уринда туради. Шифохонада ЮИК дан улим холати умумий улимлар сонининг 30-50% ни ташкил этади.
Юрак ритми ва утказувчанликниг бузилиши миокард инфарктига чалинган беморларнинг 90% да учрайди.

Сердечно-сосудистые заболевания широко распространены по всей мире в том числе и в Узбекистане. Ишемическая болезнь сердца и аритмии занимают ведущее место среди причин, приводящих к инвалидности и смерти среди населения Республики. Смертность от ишемической болезни сердца в стационарах составляет 30-50% от общей смертности.
Инфаркт миокарда считается пограничным некрозом сердечной мышцы, вызванным острым нарушением баланса между ее кровоснабжением и спросом. Нарушения сердечного ритма и проводимости встречаются у 90% больных, перенесших инфаркт миокарда.

Cardiovascular diseases are widespread all over the world, including in Uzbekistan. Coronary heart disease and arrhythmias occupy a leading place among the causes leading to disability and death among the population of the Republic. Mortality from coronary heart disease in hospitals is 30-50% of the total mortality.
Myocardial infarction is considered a borderline necrosis of the heart muscle caused by an acute imbalance between its blood supply and demand.
Cardiac arrhythmias and conduction disorders occur in 90% of patients who have suffered a myocardial infarction.

INTRODUCTION

Globally, ischemic heart disease (IHD) is the leading cause of morbidity and mortality (1). Among the atherosclerotic coronary artery diseases (CAD), the most life-threatening is acute myocardial infarction (AMI) and its associated complications. However, the majority of deaths in AMI are due to arrhythmias, which ranging from bradyarrhythmias, atrioventricular (AV) block, supraventricular tachyarrhythmias, and ventricular arrhythmias (VA) (2-3). In addition to the arrhythmias observed in the acute phase of myocardial infarction, the reopening of an infarct-related artery may increase the risk of arrhythmias even further and serious arrhythmias may appear, which increases the mortality risk (4).

Sudden cardiac death (SCD) in the setting of an acute myocardial infarction (MI) is most frequently the result of a ventricular tachyarrhythmia. The appearance of a sustained ventricular tachyarrhythmia following an MI, such as ventricular tachycardia (VT) or ventricular fibrillation (VF), in the early period post-MI may be the harbinger

of ongoing myocardial ischemia, the development of proarrhythmic myocardial scar tissue, elevated sympathetic tone or increase in circulating catecholamines, or an electrolyte disturbance such as hypokalemia. In-hospital mortality approaches 20 percent or more in patients who develop VT or VF following an MI. As such, rapid identification and treatment of these arrhythmias can be life-saving. Although all patients with a prior MI have an elevated risk of malignant arrhythmias, the magnitude of risk varies from patient to patient, with reduced left ventricular ejection fraction being the most prominent risk stratifier.

Frequent ventricular premature beats (VPBs), VT, and ventricular fibrillation (VF) are all associated with increased long-term mortality following acute MI. An acute MI may be an ST-segment elevation MI (STEMI) or non-ST-segment elevation MI (NSTEMI). Most of the data available are in patients with a STEMI. While the data may also apply to patients with an NSTEMI, information in these patients is more limited. The following is a summary of the multi-modality approach to prevention of ventricular arrhythmias following MI (STEMI), which includes treatment of ischemia, electrolyte supplementation (if needed), and beta blockers

Revascularization/treatment of myocardial ischemia — Patients with ventricular arrhythmias, especially polymorphic VT, in the setting of an acute MI should receive aggressive treatment for both the arrhythmia and myocardial ischemia. Therapy for ischemia usually includes drugs (eg, beta blockers, nitrates) and in most cases primary percutaneous coronary intervention or far less frequently, coronary artery bypass grafting for revascularization (5). Fibrinolytic therapy is also effective but is used infrequently and generally only when PCI is not immediately available.

Electrolyte supplementation — In the post-MI setting, we maintain levels of serum potassium ≥4 mEq/L and serum magnesium ≥2 mg/dL.

Hypokalemia is a risk factor for VF in the setting of an acute MI, and concomitant hypomagnesemia, which is detected in approximately 40 percent of cases of hypokalemia, prevents the correction of hypokalemia (6).The MAGIC trial showed no benefit to empiric magnesium supplementation in acute MI patients (8).Beta blockers — Oral beta blockers are administered universally to all patients without contraindications who experience an acute MI (9). In addition to other beneficial effects, the immediate administration of a beta blocker during an acute MI reduces the risk of VF. In a systematic review, the overall mortality in 31 long-term trials that included almost 25,000 patients was 9.7 percent; beta blockers reduced the odds of death by 23 percent (95% CI 15-31 percent) (10). These benefits are seen following both STEMI and NSTEMI (11).

Beta blockers are of use as the etiology of ventricular arrhythmia in the early or acute stages of an MI is in part related to enhanced automaticity, resulting from elevated catecholamines and beta receptor stimulation.

Antiarrhythmic drugs - do not administer prophylactic antiarrhythmic agents in the post-infarction period.

- The prophylactic administration of class IC antiarrhythmic agents (eg, encainide, flecainide) in the post-MI period is associated with increased mortality and is **not** recommended (12-14).
- Due to the suggestion of possible harm and unsure benefit, the routine prophylactic administration of lidocaine in the acute MI period is **not** recommended (15).
- Unlike the other antiarrhythmic drugs, prophylactic amiodarone is not associated with an increase in mortality. However, its unselected use in all patients does not appear to improve outcomes. As such, we do not administer prophylactic amiodarone in the post-MI period.

The use of these agents is reserved for patients with documented ventricular tachyarrhythmias.

Heart failure therapy — Although not considered antiarrhythmic drugs, angiotensin converting enzyme (ACE) inhibitors, aldosterone antagonists, angiotensin II receptor blockers (ARBs), and combination ARB and neprilysin inhibitor all reduce the incidence of SCD in patients with heart failure (HF). Reduced SCD rates have been reported specifically in post-MI populations with ACE inhibitors and aldosterone antagonists, and in a broader population of HF patients, approximately 50 percent of whom had a prior infarction, with an ARB.

Wearable defibrillator for primary prevention — Among patients with left ventricular ejection fraction (LVEF) ≤35 percent who are less than 40 days post-MI, we discuss the potential benefits and risks of wearable cardioverter-defibrillator (WCD) use and consider providing it to motivated patients with NYHA functional class II or III, or LVEF <30 percent and in NYHA class I, as these patients would be candidates for implantable cardioverter-defibrillator (ICD) implantation after 40 days. However, one study has not shown improvement in mortality in such patients as a result of WCD use (16). In another analysis of this trial, it was reported that the lack of benefit might be in part related to poor compliance among patients prescribed the WCD (17).

TREATMENT

Ventricular premature beats — In the post-MI patient with ventricular premature beats (VPBs) that cause significant or disabling symptoms (eg, palpitations, lightheadedness), beta blockers are administered, although most patients will already be taking them. In the rare circumstance that more aggressive antiarrhythmic therapy is considered for control of refractory symptoms, we prefer amiodarone, as it is likely to be effective and unlikely to cause significant harm, although there is an appreciable incidence of side effects with long-term amiodarone therapy. Mexiletine, which is a class IB agent that resembles lidocaine, also appears safe in the post-MI patient, and although there are no randomized trials in this population, it may be effective for arrhythmia suppression (18,19).

There is no role for chronic antiarrhythmic drug therapy to suppress asymptomatic VPBs.

VPBs, particularly if frequent (more than 10 per hour) or complex (ie, couplets or non-sustained ventricular tachycardia) appear to be associated with a worse prognosis in patients with a prior MI. Based upon this association, trials of both class I and class III antiarrhythmic medications were conducted to determine if suppression of ventricular ectopy would reduce SCD. Patients with frequent asymptomatic VPBs post-MI were randomly assigned to receive suppressive antiarrhythmic therapy or placebo in an effort to suppress the ectopy (12,13).

•The CAST study, which randomly assigned patients to treatment with encainide, flecainide, moricizine, or placebo, was prematurely terminated when it was noted that, despite suppression of VPBs, total mortality among the patients receiving encainide and flecainide was significantly **increased** compared with those on placebo (7.7 versus 3.0 percent); this was due primarily to an excess in arrhythmic deaths.

•The CAST II study, which limited treatment to moricizine or placebo, was also terminated early due to an increased risk of death or cardiac arrest in the first 14 days of therapy among patients treated with moricizine (2.6 versus 0.5 percent with placebo) (13).

•The CAMIAT study, which randomly assigned patients with frequent (≥10 per hour) or repetitive VPBs to amiodarone or placebo (approximately 60 percent were also treated with a beta blocker), showed that although arrhythmia suppression was more common with amiodarone (84 versus 35 percent with placebo), there was no significant difference in yearly all-cause or cardiac mortality (4.0 versus 5.2 percent) (20).

Nonsustained VT — For patients with symptomatic (eg, palpitations, lightheadedness) nonsustained ventricular tachycardia (NSVT) after an MI, beta blockers are administered, although most patients should already be taking them. If antiarrhythmic drug therapy is considered due to persistent symptoms, we prefer amiodarone, as it is likely to be effective and unlikely to cause significant harm, although there is an appreciable incidence of side effects with long-term amiodarone therapy. An alternative agent is mexiletine as it is safe and has been found to be effective for arrhythmia suppression in other groups of patients (18,19).

In the absence of data specific to patients with NSVT, we do not prescribe chronic antiarrhythmic drug therapy to suppress asymptomatic NSVT. The presence of NSVT in post-MI patients with an LVEF ≤40 percent is an indication for further risk stratification, if the patient does not already meet criteria for ICD placement (LVEF ≤30 percent without heart failure symptoms, or LVEF ≤35 percent with NYHA class II or III heart failure). Electrophysiologic testing prior to hospital discharge may be appropriate in patients with late NSVT (ie, more than 24 to 48 hours into acute MI).

The development of NSVT one week or later post-MI carries at least a twofold increase in the risk of SCD (21). The risk of NSVT is even further increased in post-MI patients with significantly diminished LV function (LVEF less than 40 percent). In this setting, the risk of SCD is increased more than fivefold (21,22).

Large randomized trials of antiarrhythmic drugs limited to patients with NSVT have not been performed. However, many of the patients included in the CAST and CAMIAT (39 percent) trials had NSVT. These trials showed an increased mortality in patients treated with class IC antiarrhythmic medications (12) and no significant reduction in overall mortality with amiodarone (20).

Accelerated idioventricular rhythm — An accelerated idioventricular rhythm (AIVR), which has also been called "slow VT," arises below the atrioventricular (AV) node and has, by definition, a rate between 50 and 100 beats/minute. Most episodes are transient, benign, and require no treatment. Furthermore, pharmacologic therapy is contraindicated if there is complete heart block and an escape ventricular rhythm (which is not actually AIVR), since suppression of the pacemaker focus can result in profound bradycardia and possibly asystole.

AIVR is most often seen in the peri-infarction period. AIVR often occurs after reperfusion therapy (PCI or fibrinolytic therapy) and is felt to be a reperfusion arrhythmia. AIVR occurring after the peri-infarction period is uncommon. When it occurs, reversible causes should be sought such as digitalis toxicity, hypokalemia, or hypomagnesemia. There are no convincing data linking AIVR to sustained VT, ventricular fibrillation (VF), or a worse prognosis. Thus, no therapy is warranted for asymptomatic arrhythmias, while symptomatic arrhythmias can be treated with antiarrhythmic drugs or perhaps ablation.

Polymorphic VT — Polymorphic VT associated with a normal QT interval is an uncommon arrhythmia following an acute MI. When it occurs, it is often associated with signs or symptoms of recurrent or ongoing myocardial ischemia (23). Even if there are no signs or symptoms of myocardial ischemia, underlying myocardial ischemia is the most likely etiology. If polymorphic VT lasts for more than 8 to 10 seconds, it often degenerates into VF. This type of polymorphic VT generally fails to respond to class I antiarrhythmic drugs, magnesium, or overdrive pacing but may respond to intravenous amiodarone or lidocaine (23). In patients treated with primary percutaneous coronary intervention who then manifest polymorphic ventricular tachycardia , revisualization of the coronary arteries is frequently warranted. An intraaortic balloon pump or other mechanical unloading therapy may help stabilize these patients.

Revascularization has traditionally been considered to be adequate therapy for polymorphic VT due to ischemia in the absence of acute MI. However, more recent data suggest that ICD implantation in addition to revascularization may be optimal (24).

There is a second form of polymorphic VT that develops during the healing phase (at 3 to 11 days) and occurs in association with QT prolongation (25). This arrhythmia resembles an acquired long QT syndrome and is treated in a similar fashion. One report of eight such patients found that defibrillation (if the arrhythmia is sustained), magnesium, lidocaine, beta blockers, and rapid overdrive pacing were effective therapies (26). Mexiletine, which is similar to lidocaine but is an oral medication, may be of benefit. In general, the QT interval shortened within 10 days, and long-term outcomes were uneventful.

More commonly, polymorphic VT results from either acquired or congenital long QT interval and in this situation it is called torsades de pointes. Acquired QT prolongation may result from class IA or class III antiarrhythmic drugs, which can prolong the QT interval. An exception is amiodarone, which rarely produces torsades de pointes when used alone. Amiodarone should be discontinued if the burden of polymorphic VT increases, which is a possible sign of proarrhythmia. Many other drugs, including antibiotics, psychotropic agents, antihistamines, and GI medications may prolong the QT interval. Magnesium supplementation may be of benefit, even in the absence of hypomagnesemia. Bradycardia frequently facilitates the initiation of torsades de pointes VT in a susceptible patient as the QT interval lengthens further with slower heart rates. Temporary pacing may help prevent recurrent episodes.

Withdrawal of cardiac vagal activity is considered as one of the important triggers for acute myocardial infarction (MI)-induced ventricular arrhythmias in type 2 diabetes mellitus (T2DM). Our previous study demonstrated that cell excitability of cardiac parasympathetic postganglionic (CPP) neurons was reduced in T2DM rats. This study investigated whether cell excitability of CPP neurons is associated with cardiac vagal activity and MI-induced ventricular arrhythmias in T2DM rats.

SUMMARY

- The incidence of arrhythmias within 24 hours of hospitalization in patients with STEMI undergoing primary PCI is as high as 89.1%, and it has been observed to be associated with an increased rate of in-hospital mortality.
- Patients with ventricular arrhythmias, especially polymorphic VT, in the setting of an acute MI should receive aggressive treatment for both the arrhythmia and myocardial ischemia. Therapy for ischemia usually includes drugs (eg, beta blockers, nitrates) and either primary percutaneous coronary intervention or coronary artery bypass grafting for revascularization.
- Other therapies that reduce ventricular arrhythmias during and immediately after acute MI include maintaining levels of serum potassium ≥4.0 mEq/L and serum magnesium ≥2.0 mg/dL, administering beta blockers, and appropriate therapies for heart failure, when present.
- The prophylactic administration of antiarrhythmic agents to asymptomatic patients during and immediately after acute MI has at best no benefit and

potentially can cause harm. The use of these agents is reserved for patients with documented ventricular tachyarrhythmias.

- In the post-MI patient with ventricular premature beats or nonsustained VT that cause significant or disabling symptoms (eg, palpitations, lightheadedness), beta blockers are administered, although most patients will already be taking them. In the rare circumstance that more aggressive antiarrhythmic therapy is considered for control of refractory symptoms, we prefer amiodarone, as it is likely to be effective and unlikely to cause significant harm.
- The reduction of CPP neuron excitability is involved in decreased cardiac vagal function, including cardiac parasympathetic activity and vagal control of ventricular function, which is associated with MI-induced high mortality and malignant ventricular arrhythmias in T2DM.

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