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Comparison of the effectiveness of non-ischemic therapy with a variety of basic drugs in patients with unstable angina

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Abstract
We analyzed the effect of non-ischemic therapy based on variety of basic drugs for the treatment of unstable angina pectoris. The study involved 94 patients - men and women aged 59 to 74 years (mean age of patients were 67, 2 ± 5, 2 years). All patients diagnosed with unstable angina (UA). We compared the efficacy of antianginal therapy, which includes Aspirin, Beta-blockers (Bisoprolol), Statins (Atorvastatin), Nitrates (Cardiket), ACE inhibitors (Enalapril) (I group of patients) with antianginal therapy including Aspirin, Clopidogrel, Beta-blockers (Nebivolol), Statins (Rosuvastatin), Nitrates (Cardiket), ACE inhibitors (Enalapril), and L-arginine (II group of patients). All patients were assessed for dynamic clinical condition, ectopic activity and myocardial ischemia, Holter ECG monitoring were used. The treatment results were evaluated after 20-21 days at the end of treatment. The criteria for assessing the effectiveness was the reduction of the number of angina attacks at the end of the treatment, reducing the number of nitrates tablets cupping, reducing episodes of silent myocardial ischemia (SMI), the pain of myocardial ischemia (PMI), the number of supraventricular complex (PVC) and ventricular premature beats (VC) were monitored on a daily basis by the use of Holter ECG (electrocardiogram HM).
During treatment of the 1st group of patients, the number of angina attacks that needed nitrates, decreased by 56% from the third week of treatment: in 28 patients (61%) the number of angina attacks decreased by more than 50%, in 18 pts decreased by less than 50%. At the end of the treatment in patients of the main comparative group the number of angina attacks that needed taking nitroglycerin, decreased by 67%:in 36 patients (75%) the number of angina attacks decreased by more than 50%, in 12 pts decreased by less than 50%.
The treatment of patients showed pronounced antianginal and anti-ischemic effects: daily amount of pain episodes of myocardial ischemia (PMI), and silent myocardial ischemia (SMI) and the total duration of the data of ECG HM significantly reduced in both groups of patients. The total daily duration of SMI in the main second group patients with unstable angina after treatment became 2.3 times less compared with first group of patients. The total daily duration of BIM in patients with II group became 1.3 times less appeared than in compared patients after treatment.
In the comparative group of patients at the end of treatment the daily amount of supraventricular episodes reduced at least in 2 times, while in patients of main group - 3.2 times. The daily number of VCs in patients with the complex treatment became 1.7 times less compared with usually treated patients of the first group.
Thus, more intensive complex treatment of unstable angina with L-arginine leads to beneficial optimization of myocardial ischemia parameters

Keywords: Unstable angina, myocardial ischemia, pain, silent myocardial ischemia, supraventricular arrhythmias, ventricular premature beats, antianginal therapy.

Introduction

Problem formulation

Study of pathogenic stable and unstable coronary heart disease (CHD) and optimization of the treatment of patients with this pathology remain relevant in the field of view of scientists all over the world. Obviously, the structure of cardiovascular disease CHD, along with hypertension and cerebrovascular disease are the leading cause of mortality and disability [27]. The prevalence of these disorders increases among the population in general and in Ukraine in particular [6, 16, 25],that creates a major health and social problem.
Previous studies of essential disorders of cellular and humoral immunity [14, 19, 22, 31], the fatty acid spectrum (CSW) platelet membrane [1, 7, 20, 21], FSW lymphocyte membranes [3, 13, 18] and amino acid spectrum of blood plasma [4, 15, 17] have shown a remarkable importance in the development of a stable and emergency situations. We already have analyzed the effect of antianginal therapy on these parameters: it have proved an advantage to use the combination of antiplatelet therapy on the impact of immunological status [8, 9], FSW platelet membrane [1, 11], FSW lymphocyte membranes [5], ectopic activity and myocardial ischemia [10, 12, 23]. The effectiveness of adding L-arginine to antianginal therapy is seen in the content of essential amino acids (AA) in blood plasma [2, 30, 33].
The results and clinical experience shows the advantages of rosuvastatin when compared with atorvastatin [26, 28, 29] and nebivolol compared with other beta-blockers [24, 32], so it is reasonable to study the treatment with various antianginal drugs representatives in patients with unstable angina.

Purpose of the study

To compare the efficacy of antianginal therapy, which includes trivial therapy with Aspirin, Bisoprolol, Atorvastatin, Cardiket, Enalapril with concomitant Antianginal therapy including Aspirin, Clopidogrel, Nebivolol, Rosuvastatin, Cardiket, Enalapril, and L-arginine in patients with unstable angina by monitoring general clinical condition, ectopic activity and myocardial ischemia.

Object of study

Unstable patients with silent myocardial ischemia, myocardial ischemia, pain, supraventricular arrhythmias, and ventricular arrhythmia according to daily monitoring of ECG Holter.

Material and Methods

We examined 94 patients - men and women aged 59 to 74 years (mean age of patients was 67, 2 ± 5, 2 years). All patients were diagnosed with unstable angina according to international guidelines and local Order of Ministry of Health № 436 "On Approval of the requirements for medical care in the "Cardiology" specialty. The study did not include patients with severe heart failure, atrial fibrillation, and concomitant disorders in the stage of decompensation, cancer, diseases of the musculoskeletal system.

All the patients were divided into two groups. The first group of patients (n=46) received antianginal therapy including Aspirin 75 mg, Bisoprolol 5 mg, Atorvastatin 10 mg, Cardiket 20 mg twice a day, nitroglycerine for relief of angina attack, Enalapril 10 mg twice a day. The main second group of patients (n=48) received antianginal therapy including Clopidogrel 75 mg with Aspirin 75mg, Nebivolol 5 mg, Rosuvastatin 10 mg, Nitrates 20 mg twice a day, nitroglycerin for relief of angina attacks, Enalapril 10 mg twice a day and L- arginine (Tivortin by Yuri-Farm) 100 ml intravenously daily (a total of 6 injections). All patients were given dietary advice and recommendations on lifestyle modifications and the rejection of bad habits.

Observations were carried out before and after treatment (after 22-21 days). The criterion for assessing the effectiveness at the end of the treatment was the number of angina attacks, reducing the number of nitroglycerin tablets, reducing episodes of SMI, PIM, as the number and PVCs according to the daily Holter ECG monitoring (HM ECG). In particular were analyzed the total number of rare PVCs (RPVC), coupled PVCs (CPVC), the group PVCs (GPVC), rare VCs (RVC) coupled VCs (CVC), group VCs (GVC).

The results were processed on a PC using the Microsoft Office software package. Statistical analysis of the data used by the program Microsoft Excel 2010. The significance of differences between the average performance of different groups provided by determining the Student t-test or Pearson.

Results and Discussion

According to the dynamics of the average number of angina attacks and the number of nitroglycerin tablets a week, it was revealed a progressive decrease between two groups of patient since the third day of treatment. The number of angina attacks that needed taking nitroglycerin, decreased by 56% for the third week of treatment in patients of the first group: in 28 patients (61%) of the number of angina attacks decreased by more than 50%, in 18 decreased by less than 50%. In patients of the main second group the number of angina attacks that needed taking nitroglycerin, decreased by 67%:in 36 patients (75%) of the number of angina attacks decreased by more than 50%, in 12 decreased by less than 50%.

The intensive treatment provided marked antianginal and anti-ischemic effects: daily number of episodes of SIM and the PMI and the overall duration of ischemic ECG data significantly decreased in both groups of patients, as shown in Tables 1, 2.

Table 1. Comparative characteristics of the Silent Myocardial Ischemia according to Holter ECG in patients with unstable angina before and after treatment, (M ± m).

Indicator	Before Treatment (1)	After Treatment		P1-2	P1-3	P2-3
		I Group (2)	II Group (3)			
No. of Episodes	6,1±0,5	3,5±0,05	1,8±0,06	<0,01	<0,01	<0,05
Overall time (minutes)	137,4±14,3	67,2±6,5	30,6±3,6	<0,01	<0,01	<0,01
Depth ↓ST (мм)	2,7±0,2	0,9±0,06	0,4±0,05	<0,01	<0,01	>0,05

The advantage in antinational therapy in patients realized in significant decrease in the number and duration of episodes of SMI recorded during the day in both groups as compared with those before treatment. The total number of episodes in patients with SMI of the group I after treatment decreased from 6.1 to 3.5 (42.7%) as for patients of II group SMI number of episodes decreased from 6.1 to 1.8 (48.6%), (p<0.01). Duration of SMI for the I group decreased from 137.4 to 67.2 (51.1%) after treatment in comparison with 137.4 to 30.6 (77.8%) for group II, p<0.01. The depth of the ST segment in patients from both groups significantly decreased after treatment (P<0.05).

Significant difference between the two groups of patients after treatment have been identified in the number of episodes in patients of the first group with SMI after treatment as shown in Table 2 was reduced from 2.2 to 1.0 (45.5%) and main patients group decreased from 2.2 to 0.9 (59.1%)., p<0.01. The duration of SMI in patients of I group after treatment decreased from 46.8 to 22.6 (51.8%) and patients of II group from 46.8 to 16.7 (64.4%), p<0.01. In Group II, the total duration of episodes of SMI significantly decreased by 26.1% (p<0.05) in comparison with I group of patients. The depth of the ST segment in patients from both treatment groups significantly decreased after treatment (P<0.05). Significant difference between two treatment groups in the number of episodes of SMI and the depth of ST segment after treatment have been identified.

Table 2. Comparative characteristics of episodes of SMI according to HM ECG in patients with UA groups I and II before and after treatment, (M ± m)

Indicator	Before Treatment(1)	After Treatment		P(1-2)	P(1-3)	P(2-3)
		I Group (2)	II Group (3)			
No. Of Episodes	2,2±0,04	1,2±0,08	0,9±0,08	p<0,01	p<0,01	>0,05
Overall Time (minutes)	46,8±8,3	22,6±2,1	16,7±2,2	p<0,01	p<0,01	p<0,05
Depth ↓ST (мм)	2,3±0,2	0,9±0,07	0,8±0,08	p<0,05	p<0,05	>0,05

Table 3. The frequency of registration of cardiac arrhythmias during the day according to HM ECG in patients with HC after treatment, (M ± m)

Type of Arrhythmia	Before Treatment (1)	After Treatment		P1-2	P1-3	P2-3
		I гр. (2)	II гр. (3)			
RVC	126,5±20,1	69,2±11,1	39,2±6,7	<0,01	<0,01	<0,01
CVC	5,2±1,1	2,5±0,08	1,2±0,09	<0,05	<0,05	<0,05
GVC	8,3±1,8	4,6±0,7	2,1±0,07	<0,05	<0,05	<0,05
RPVC	71,2±10,5	34,5±4,3	21,5±2,2	<0,01	<0,01	<0,05
CPVC	4,7±1,4	2,5±0,3	1,5±0,08	<0,05	<0,05	>0,05
GPVC	3,2±0,9	2,3±0,5	1,2±0,06	>0,05	<0,05	<0,05

A significant influence of the treatment on the electrical instability of the myocardium in examined patients for groups I and II, as shown in Table 3.

As the two groups of patients after treatment recorded significantly lower daily amount (RVC) compared with before treatment (126, 5 ± 20, 1 and 69, 2 ± 11, 1, p<0, 01; 126, 5 ± 20, 1 and 39, 2 ± 6, 7, p<0.01). It should be noted that the Group II patients after treatment registered a significant reduction in the amount (RVC) as compared with before the treatment, respectively, 45.3% and 69.1%. 71, 2 ± 10, 5 and 34, 5 ± 4, 3, p<0.01, respectively). After the treatment in both groups was recorded significantly fewer PNSHE (71,2 ± 10,5 and 34,5 ± 4,3, p<0,01; 71,2 ± 10,5 and 21,5 ± 2,2 p<0.01, respectively).

Attention is drawn to the fact that the patients of group II a significant reduction in the number of RPVC than patients in group I as compared with before treatment, respectively, 69.9% and 51.6%. Importantly, patients with I and II significantly decreased the amount of GVC as compared with before the treatment (and 8,3 ± 1,8 4,6 ± 0,7, p<0.05; and 8,3 ± 1,8 2,1 ± 0,07, p<0.05, respectively). And it is more significant decrease in patients with Group II respectively 44.6% and 74.7%. It should be noted that patients with Group II., In contrast to the patients of the I c., After the treatment significantly decreased the number of GPVC In both groups of patients also reported a significant decrease in the number of GPVC as compared with before treatment (3, 2 ± 0, 9 and Feb. 1 ± 0, 06, p<0, 05; 3, 2 ± 0, 9 and 2, 3 ± 0,5, p> 0.05).

Conclusion

1. In unstable angina patients receiving basic therapy, including ASA-Aspirin, Bisoprolol, Atorvastatin, Cardiket, Enalapril daily number of episodes of SMI decreased by 1.7 times, while in patients treated with Clopidogrel, Acetylsalicylic acid, Nebivolol, Rosuvastatin, Cardiket, Enalapril and L-arginine - 3.4 times. The daily amount of SMI in patients with complex treatment was the half less compared with patients of usual treatment group.
2. The total daily duration of SMI in the I group with unstable angina decreased by 2 times, and in the group II. - 4.5 times. The total daily duration of SMI in patients after treatment became 2.3 times less when compared with patients of group 1.
3. Patients with HC treated with basic therapy including Aspirin, Bisoprolol, Atorvastatin, Cardiket, Enalapril daily number of episodes BIM decreased by 1.8 times, and in patients treated with clopidogrel, acetylsalicylic acid, nebivolol, Rosuvastatin, Cardiket, Enalapril and L-arginine (Tivortin) - 2.4 times. The daily amount of BIM in patients with Group II. It became 1.3 times less when compared with patients of group 1
4. The total daily duration of BIM in I patient group decreased by 2.4 times, and in II patients group - 2.8 times. The total daily duration of BIM in I group with after treatment became 1.3 times less when compared with II group.
5. Patients with unstable angina treated with basic therapy including Aspirin, Bisoprolol, Atorvastatin, Cardiket, Enalapril daily amount PVCs decreased by 1.8 times versus patients treated with Clopidogrel, Acetylsalicylic acid, Nebivolol, Rosuvastatin, Cardiket, Enalapril and L arginine - 3.3 times. The daily number of PVCs in group II became 1.7 times less compared with I group.
6. Patients with unstable angina at the end of treatment the daily amount reduced 2 times, while in II group - 3.2 times. The daily number of PVCs in patients with Group II became 1.7 times less compared with group 1.
7. More intensive complex treatment of unstable angina with L-arginine lead to beneficial optimization of myocardial ischemia parameters.

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