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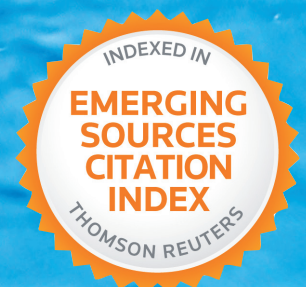
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ABSTRACT

Aim: The purpose of the work was to study the possibility of using Dihydroquercetin in rehabilitation programs for patients with coronary artery disease after Coronary artery bypass grafting (CABG) surgery in order to increase the effectiveness of rehabilitation, which has notable scientific and practical significance.

Materials and Methods: The methodological basis of the research is based on systemic, historical, terminological, and informational approaches.

Results: The results of the study showed the high clinical effectiveness of Dihydroquercetin in the complex medical rehabilitation of patients with coronary artery disease who underwent the operation. The pill intake did not affect indicators of carbohydrate and lipid metabolism, which indicates its metabolic neutrality. None of the patients had any worsening of the condition, increased frequency of angina attacks, or episodes of painless ischemia. All patients indicated good tolerability of the drug, and improvement in general well-being (reduction or disappearance of shortness of breath, decrease in pain intensity, increase in activity, improvement in sleep). The implementation of the optimized rehabilitation program also contributed to the improvement of the psycho-emotional state of the patients.

Conclusions: Complex medical rehabilitation of patients with coronary heart disease after Coronary artery bypass grafting surgery according to a program with the inclusion of Dihydroquercetin helps to improve the rheological properties of blood, strengthen the active vasomotor mechanisms of MC regulation, improve indicators of central and peripheral hemodynamics, blood oxygenation, increase in exercise tolerance, improve psycho-emotional the condition, which ultimately ensure an increase in the rehabilitation effect.

KEY WORDS: ischemic heart disease, dihydroquercetin, biologically active supplements

INTRODUCTION

The state of health of the population is one of the most important factors in the economic development and well-being of the country. This social trend is supported by legislative documents that regulate the development and implementation in the coming years of new technologies for expanding the range and production of healthy food products with certain quality characteristics. Chronic deficiency of essential trace elements in the diet of a modern person against the background of disturbances in the structure of nutrition, hypo dynamism, adverse environmental factors, and other adverse effects of civilization is associated with the occurrence of general diseases and leads to a decrease in the duration of working capacity and unjustified socio-economic losses. Available domestic and international experience shows that the problem of

optimizing nutrition, including the diet special products containing biologically active additives (BAA), with a targeted systemic effect, convincingly indicates a successful solution to health problems. Therefore, the development of scientific principles, recipes, and technologies, supported by studies of quality indicators and an evidence base of effectiveness, is relevant and timely.

Dietary supplements (naturopathic remedies) are, as a rule, concentrates identical to natural biologically active substances, obtained as a result of processing plant and animal raw materials. Biologically active substances include dihydroquercetin, also known as "taxifolin" in Europe, which refers to natural antioxidants, or bioflavonoids. Dihydroquercetin is widely used in the production of biologically active supplements due to its excellent antioxidant and capillary protective properties.

Dihydroquercetin is often combined with vitamins, mineral complexes, and extracts of medicinal plants, creating vitamin drinks and cocktails for improving well-being in nutrition and rehabilitation practices.

Despite significant achievements in the field of pharmacotherapy of patients with coronary heart disease (CHD), surgical treatment of this category of patients, in particular, direct myocardial revascularization surgery - coronary artery bypass grafting (CABG), in some cases is the most effective [1-3]. As a result of the operation, coronary blood flow is restored, which eliminates or reduces myocardial hypoxia [4-6]. However, surgical treatment does not eliminate the main causes of the disease, it can be considered only as one of the stages in the complex treatment of CAD. In addition, severe surgical trauma, such as CABG surgery, naturally causes complex and diverse body reactions [2, 6, 7]. Being protective and adaptive in nature, they can acquire a pathological character and manifest themselves in various complications both immediately after the intervention and in the later rehabilitation period.

Overcoming the consequences of surgical intervention, prevention, and treatment of early and late postoperative complications largely determine the effectiveness of the entire complex of rehabilitation measures [1-5]. The analysis of data from the literature [1, 2, 7] and the results of our own research [3, 4, 6] made it possible to reveal a number of regularities of the clinical course and pathogenetic changes accompanying the postoperative period in patients with coronary artery disease, which is characterized by the following main syndrome complexes: cardiac, post-sternotomy, respiratory, hemorheological with impaired microcirculation, psychopathological, hypodynamic, metabolic, post-phlebotomy. Of great importance is the hyperthrombotic syndrome, which is characterized by pronounced changes in blood coagulation and anticoagulation, hematocrit parameters, fluidity limit, blood viscosity, and an increase in the functional activity of platelets [2, 4, 8]. A significant increase in the level of fibrinogen, as well as a significant increase in the content of soluble fibrinogen and fibrinogen-fibrin degradation products, indicates an increase in blood coagulation potential in patients with coronary heart disease. Violation of the rheological properties of blood leads to a decrease in oxygen supply to tissues [3].

In addition, patients with coronary heart disease after CABG surgery in the postoperative period show signs of disseminated intravascular coagulation syndrome, the development of which also contributes to the disruption of blood microcirculation (MC), in connection with which the search for new means that contribute to its improvement is urgent. Such means include the bioflavonoid Dihydroquercetin, which is obtained from the wood of Daurian larch and Siberian larch. Dihydroquercetin has a stimulating effect on tissue blood flow, stabilizes the barrier function of microvessels, reduces the permeability of capillary walls, and thus contributes to the reduction of stagnant phenomena in the microcirculatory channel.

AIM

The purpose of the work was to study the possibility of using Dihydroquercetin in rehabilitation programs for patients with coronary artery disease after CABG surgery in order to increase the effectiveness of rehabilitation, which has great scientific and practical significance.

MATERIALS AND METHODS

The material of the study was the results of observation, examination and rehabilitation of 30 patients with coronary heart disease who underwent CABG surgery and arrived at the Department of rehabilitation of Public non-commercial enterprise Ivano-Frankivsk regional cardiology dispensary of the Ivano-Frankivsk regional council on the 12th–17th day (on average - 15.2 days) after surgical treatment. The age of the patients ranged from 32 to 68 years (on average - 47.6 ± 3.2 years). The age group of 41–50 years was the most numerous.

The study was carried out in compliance with the basic provisions of the "Rules of ethical principles of scientific medical research with human participation", approved by the Declaration of Helsinki (1964-2013), ICH GCP (1996), EEC Directive No. 609 (dated 24.11.1986), Orders of the Ministry of Health of Ukraine No. 690 (dated 23.09.2009), No. 944 (dated 14.12.2009), No. 616 (dated 03.08.2012). All the participants were informed about the goals, organization, methods of examination and signed an informed consent to participate in the completely anonymous study.

The methodological basis of the research is based on systemic, historical, terminological and informational approaches. The systemic approach made it possible to simultaneously present physical rehabilitation/physical therapy for cardiovascular system disorders as a complex and integral object with the coordinated functioning of all parts and a set of sequential actions, most of which are performed together by a doctor of rehabilitation medicine, a physical therapist, and a patient. The use of the terminological approach was determined by the theoretical nature of the research. There was a need to describe, clarify and define the concept of biologically active supplements that can be effectively used in the rehabilitation of patients with cardiovascular system dysfunctions. Based on the information approach and the principle of informativeness, physical rehabilitation/physical therapy for cardiovascular disorders was investigated as an information system with combined management, which transforms the input medical information about the patient into the output information about the restoration of the functions of the cardiovascular system, activity and health.

To achieve the goal, the following general scientific research methods were used: general logical - abstraction, concretization, analysis, synthesis, induction, comparison, analogy; empirical knowledge - observation (qualitative); of theoretical knowledge - definition of scientific concepts, idealization, mental modeling.

RESULTS

We studied the possibility of optimizing the medical rehabilitation of patients with coronary artery disease

after CABG surgery by improving MC with the help of Dihydroquercetin. The average number of shunts per 1 patient was 2.3 ± 0.8 . During the study of the anamnesis, it was established that 19 (63.3%) patients underwent myocardial infarction before the operation. According to the NYHA classification, upon admission, 3 (10%) patients were assigned to I functional class (FC), 10 (33.3%) to II, 15 (50%) to III, and 2 (6.6%) to IV. The vast majority of patients are employees of highly emotional mental work (Table 1).

Among concomitant diseases, the most common were hypertension - in 16 (39.5%) patients, obesity - in 8 (26.6%), peptic ulcer - in 5 (16.6%), chronic bronchitis - in 6 (20%), chronic gastroduodenitis in 7 (23.3%), type 2 diabetes mellitus in 3 (10%). Most patients systematically smoked 20 to 40 cigarettes per day. Of the early postoperative complications affecting the course of rehabilitation, heart rhythm disturbances, complications from postoperative wounds, reactive pericarditis, and hydrothorax were noted. At the rehabilitation stage, patients most often complained of shortness of breath during normal physical exertion,

general weakness, pain along the course of the postoperative sternum scar, sleep disturbances. Improvement of MC after CABG surgery by improving MC with the help of Dihydroquercetin and indicators of FEB contributed to the positive dynamics of indicators of acid-base homeostasis (ABH) and gas composition of blood (Table 2).

As is evident from the data in Table II, patients of the main group had a more significant improvement in blood oxygenation than in controls, which was confirmed by a significant increase in PB2 and a decrease in blood PCO₂. The positive dynamics of MC indicators, improvement of blood oxygenation ensured an increase in the contractility of the myocardium, its propulsive force, a decrease in the average pressure in the pulmonary artery (AvPPA), which as a result contributed to a significant increase in exercise tolerance (ET) in the majority of patients of the main group (Table 3).

The results of the study showed the high clinical effectiveness of Dihydroquercetin in the complex medical rehabilitation of patients with coronary artery disease who underwent CABG. The drug did not affect indicators

Table 1. Dynamics of MC indicators in the rehabilitation process (M±m)

Index, points	Control group (n=10)		Main group (n=20)	
	before treatment	after treatment	before treatment	after treatment
KI	7,7±0,3	1 7,2±0,21	8,3±0,37	6,9±0,39*
KII	0,89±0,20	0,88±0,23	0,89±0,35	0,80±0,36
KIII	5,80±0,42	5,64±0,45	5,78±0,40	4,85±0,35*
KIV	0,99±0,17	0,92±0,21	0,98±0,20	0,95±0,35

Note: * - the indicated indicators may probably differ from the indicators before treatment $p < 0,05$

Table 2. Dynamics of ABH indicators and blood gas composition in the rehabilitation process (M±m)

Index	Control group (n=10)		Main group (n=20)	
	before treatment	after treatment	before treatment	after treatment
pH	7,40±0,03	7,39±0,02	7,38±0,03	7,38±0,02
PCO ₂ , mm Hg	41,4±1,34	39,4±1,44	41,4±1,44	38,3±1,33
PO ₂ , mm Hg	70,8±1,60	75,2±1,40	71,0±1,73	83,6±1,81*
Total plasma CO ₂ , mmol/liter	23,84±1,6	23,79±1,4	23,95±1,6	23,93±1,3
AB, mmol/liter	22,4±0,9	23,0±1,1	23,0±1,6	22,9±1,4
BE, mmol/liter	-2,3±0,4	-2,4±0,3	-2,4±0,4	-2,5±0,3
SB, mmol/liter	23,1±0,6	23,5±0,4	23,6±0,6	23,4±0,5

Note: * - indicators may differ from the indicators before treatment $p < 0,05$

Table 3. Changes in indicators of hemodynamics and ET during rehabilitation (M±m)

Index	Control group (n=10)		Main group (n=20)	
	before treatment	after treatment	before treatment	after treatment
Cardiac index, liter/m ²	2,78±0,22	2,80±0,25	2,71±0,12	2,66±0,15
Emission fraction, %	52,0±1,5	54,4±1,42	50,8±1,4	56,2±1,5*
Bandwidth repeater, units	1126,3±40,4	1156,7±39,8	1092,4±40,1	1001,2±39,6
AvPPA, mm Hg	23,9±5,2	18,7±5,4	24,0±3,9	17,1±3,4*
ET, W	77,4±5,1	86,3±4,4	70,7±4,3	94,3±4,2**

Notes: * - indicators may differ from the indicators before treatment at $p < 0,05$; ** - indicator may differ from the initial one at $p < 0,001$

of carbohydrate and lipid metabolism, which indicates its metabolic neutrality. None of the patients had any worsening of the condition and increased frequency of angina attacks and episodes of painless ischemia. All patients indicated good tolerability of the drug, and improvement in general well-being (reduction or disappearance of shortness of breath, decrease in pain intensity, increase in activity, improvement in sleep). The implementation of the optimized rehabilitation program also contributed to the improvement of the psycho-emotional state of the patients. Their mood improved, and the index of reactive anxiety (RA) decreased statistically significantly - from 48.2 ± 4.1 to 34.4 ± 3.0 points ($p < 0.01$); in patients of the control group, the RA indicator decreased from 46.4 ± 5.1 to 39.5 ± 4.4 points ($p > 0.05$). Statistically unreliable reduction of indicators according to the scales of the neurotic triad (from 60.1 ± 1.34 to 57.1 ± 1.37 T-score for the 1st; from 59.7 ± 1.22 to 56 , for the 2nd 5 ± 1.27 T-score, on the 3rd - from 61.4 ± 1.32 to 58.5 ± 1.35 T-score; $p > 0.05$) in patients of the main group indicates the preservation of psychological maladaptation in part of operated patients, which requires appropriate correction. The development of microcirculatory disorders in coronary heart disease, including after CABG surgery, is caused mainly by changes in the rheological properties of blood due to impaired deformability of erythrocytes, increased aggregation of them, and platelets, increased hemostatic and decreased fibrinolytic potential of the blood, latent syndrome of disseminated dynamics of microvessels, which leads to increase in the volume of the microcirculatory bed, centralization of blood flow and inefficiency of MC [4-6, 9]. Stagnation, deposition of blood in capillaries, and venules contributes to a decrease in the venous return of blood to the heart and, in connection with this, to a decrease in cardiac output and a violation of tissue oxygenation. In turn, violations of the rheological properties of blood, associated with the aggregation of erythrocytes and accompanied by a decrease in the number of the latter, further disrupt the supply of tissues with oxygen. The main cause of tissue hypoxia is the development of a mechanical microcirculatory block.

It can be assumed that pronounced violations of pulmonary ventilation in patients cause hypoxia and metabolic disorders in tissues. This leads to the appearance of a number of vasoactive substances that contribute to the development of microvascular disorders and intravascular aggregation, which, in turn, supports and increases tissue metabolism disorders. Violations of FEB, ABH, gas composition of blood and MC, hypercoagulation, and reduction of the contractility of the myocardium leading to a decrease in the reserve capabilities of the cardiorespiratory system, which is clinically manifested by a decrease in ET, respiratory and heart failure [4, 5, 6, 9]. The positive dynamics of most of the indicators of the cardiorespiratory system during the rehabilitation program with the inclusion of Dihydroquercetin indicates improvement of MC, normalization of ABH and gas composition of blood, an increase of ET, elimination, and reduction of manifestations of respiratory and heart failure in most patients.

DISCUSSION

The results of the study suggest that Dihydroquercetin indirectly affects central and peripheral hemodynamics, improves indicators of intracardiac hemodynamics, and improves FEB and blood gas composition. The drug also eliminates spasms of arteries, including coronary arteries [4]. With a pronounced atherosclerotic lesion of the coronary arteries, even minimal changes in the normal tone of the smooth muscles in the areas of narrowing can increase ischemia or contribute to its reduction. Reduction of ischemia may be a consequence of relaxation of the normal tone of the smooth muscles of the stenosed areas of the coronary arteries. In addition, taking Dihydroquercetin prevents and relieves spasms in both normal and coronary arteries affected by the atherosclerotic process and thus contributes to the elimination of microangiopathy [1, 4-10].

The mechanism of inhibition of free radical reactions, including lipid peroxidation (LPO), in the presence of Dihydroquercetin (DHQ) can be different. It is proved that Dihydroquercetin can interact with lipid radicals and reactive oxygen species, such as hydroxyl and superoxide radicals, as well as chelate transition metal ions.

It is effective in rheumatism, septic endocarditis, and vegetative dystonia. It inhibits the development of dystrophic and sclerotic processes in the eyes and increases visual acuity. Inhibits inflammatory processes, and has a decongestant effect. Favorably affects the skin, normalizes the synthesis of collagen, and elastin in the skin (eliminates acne and pustular rash, helps maintain elasticity, skin). With prolonged use, it prevents the exacerbation of chronic respiratory diseases and the occurrence of acute respiratory viral infections. Helps to maintain the functions of the immune system, and has an antitoxic effect. It has gastroprotective activity: it stimulates the processes of regeneration of the gastric mucosa, prevents the development, and/or promotes the healing of gastric and duodenal ulcers. It has a hepatoprotective (antitoxic) effect, has radioprotective activity, and reduces the adverse effects of chemotherapy and radiotherapy on the body.

Dihydroquercetin is a reference antioxidant. Its antiradical activity is manifested at a concentration of approximately 0.0001-0.00001% in the complete absence of mutagenic activity for humans. The value of DHQ in pharmacology is invaluable. It has powerful anti-inflammatory and anti-allergic properties, strengthens and restores connective tissue, helps lower cholesterol levels, enhances the effect of many beneficial substances (vitamin C, etc.); strengthens blood vessels and capillaries, improves blood microcirculation, prevents the formation of blood clots, reduces inflammation in the prostate, strengthens the immune system. Also, DHQ protects the stomach and liver from harmful effects, and activates the processes of regeneration of the gastric mucosa. It has a pronounced prevention of the main diseases of aging: cancer, cardiovascular diseases, brain diseases, etc. It increases the resistance of body tissues to the damaging effects of excess blood sugar, reduces the likelihood of diabetes, and also facilitates the course of

developed forms. It has a positive effect on the nervous system and activates the nervous processes. The regulatory effect of this substance on several reactions of the body's immune system, on the course of inflammatory processes, characterizes it as an anti-allergic and anti-inflammatory agent that can reduce the damaging effects of a variety of adverse environmental factors from industrial pollution and infectious agents to household allergens. Thus, the presence of even small amounts of Dihydroquercetin in the daily diet will ensure the prevention of entire classes of diseases, such as tumor, hereditary, and metabolic, and will also give a rejuvenating and therapeutic effect. DHQ has low intrinsic toxicity, which makes it available for

consumption in almost unlimited doses. This property DHQ is especially valuable for people suffering from allergies.

CONCLUSIONS

Thus, complex medical rehabilitation of patients with coronary heart disease after CABG surgery according to a program with the inclusion of Dihydroquercetin helps to improve the rheological properties of blood, strengthen the active vasomotor mechanisms of MC regulation, improve indicators of central and peripheral hemodynamics, blood oxygenation, increase ET, improve psycho-emotional the condition of patients, which ultimately ensures an increase in the rehabilitation effect.

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CONFLICT OF INTEREST

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