до и после использования индивидуальных шин–кап. ***Результаты работы:*** объективное исследование зафиксировало разницу в показателях расстояний между определенными точками зубов, окружающих дефект, при отсутствии деформаций зубных рядов и при их наличии (расстояние АВ в контрольной и опытной группах составила соответственно 7,16±0,19 мм и 4 , 32±0,19 мм, AD – 7,62±0,19 мм и 4,16±0,20 мм, ВС – 7,49±0,19 мм и 4,07±0,19 мм, CD – 6.96±0.19мм и 3,67±0,19 мм). После проведения подготовки к протезированию пациентов с имеющимися дефектами зубных рядов и зубочелюстными деформациями с использованием индивидуальных съемных шин–кап в несколько этапов удалось значительно уменьшить показатели расстояний при наличии патологии и приблизить их к физиологическим (АВ – 5,85±0,21 мм, AD – 6,09±0,18 мм, ВС – 6,22±0,19 мм и CD– 5,73±0,19 мм). ***Выводы:*** применение индивидуальных съемных шин–кап позволило значительно повысить эффективность протезирования путем нормализации окклюзионных соотношений и жевательной нагрузки на смещены зубы в области дефекта зубного ряда.

Ключевые слова: ортопедическое лечение, деформации зубных рядов, жевательная эффективность.

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The Efficiency of the Use of Individual Removable Dental Bite Splints for Correction of Dental Deformations Degree in Patients with Denture Defects

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Abstract. **Objective:** introduction of prevention methods and increase of the treatment efficacy of teeth deformations using individual dental bite splints. **Materials and methods:** The results of clinical examination of 67 patients of different age (20 to 59 years) with the existing dentition defects before and after use of individual removable dental bite splints are given in this article. **The results of the work:** the objective study showed a difference in data of the distances between certain points of the teeth surrounding the defect without dentition deformations and in their presence (distances AB in the control and experimental groups was respectively7.16 ± 0.19 mm and 4.32 ± 0.19 mm, AD –7.62 ± 0.19 mm and 4.16 ± 0.20 mm, BC – 7.49 ± 0.19 mm and 4.07 ± 0.19 mm, CD – 6.96±0.19 mm and 3.67±0.19 mm). After the performance of the preparation of the patients with the dentition defects and deformations of the teeth with the use of individual dental bite splints to the prosthetic repair in several stages, it became possible to reduce significantly indexes of the distances in the presence of pathology and bring them closer to physiological data (AB – 5.85 ± 0.21 mm, AD – 6.09 ± 0.18 mm, BC – 6.22 ± 0.19 mm, and CD– 5.73±0.19mm). **Conclusions:** The use of individual removable dental bite splints gave the possibility to improve significantly the prosthetic efficacy by normalizing the occlusal relations and chewing load onto the displaced teeth in the area of dentition defect.

Keywords: orthopedic treatment, deformation of dentition, chewing efficiency.

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Effects of Quercetin on Cardiac Fibrosis in Patients with Acute Myocardial Infarction and Arterial Hypertension

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Abstract. Arterial hypertension is an independent predictor of acute myocardial infarction. Nowadays, plasma levels of fibronectin and matrix metalloproteinase 9 are the markers of left ventricular remodeling.

The objective of the research was to investigate potential antifibrotic effects of Quercetin in patients with acute myocardial infarction and arterial hypertension.

Material and methods. 130 patients with myocardial infarction (63 individuals with concomitant arterial hypertension and 67 individuals without it) were observed. All the patients were divided into groups of basic treatment and additional prescription of Quercetin. Transthoracic echocardiogram was used. To evaluate plasma level of fibronectin and matrix metalloproteinase 9 the ELISA method was applied.

Results. In all the patients, a significant decrease in fibronectin plasma levels was observed since the 28th day of treatment; however, it was more significant in group of additional prescription of Quercetin. Revascularization and pharmacological management of myocardial infarction resulted in the reduction in matrix metalloproteinase 9 plasma levels in all the patients since the 7th day of treatment; however, it was more significant in group of additional prescription of Quercetin.

Conclusions. Quercetin possesses potential antifibrotic properties causing a reduction in plasma levels of fibronectin and matrix metalloproteinase 9 in patients with myocardial infarction and concomitant arterial hypertension.

Keywords: myocardial infarction; arterial hypertension; fibronectin; matrix metalloproteinase 9; Quercetin

Problem statement and analysis of the recent research

Arterial hypertension (AH) is a major cardiovascular risk factor affecting approximately 30–45% of the general population worldwide [1]. Hypertension is associated with an increased incidence of other risk factors directly contributing to the development and progression of atherosclerotic disease [2]. Accordingly, patients with myocardial infarction (MI) and a history of AH are known to be older and to have a higher rate of comorbidities and more extensive atherosclerotic disease than patients with MI and without hypertension [3]. Several studies demonstrated that patients with MI and antecedent AH are at increased risk of adverse cardiovascular events, such as heart failure, recurrent MI or even death [4, 5]. Thus, in substudy of the AIDA-STEMI trial, antecedent hypertension was associated

with a significantly increased baseline risk profile (advanced age, higher body mass index, higher incidence of diabetes mellitus, hypercholesterolemia, previous angioplasty and multivessel disease, p<0.001 for all). Major adverse cardiovascular events (MACE) were more frequent in patients with hypertension as compared to patients without hypertension (45 (8%) vs. 8 (3%), p<0.01). AH remained an independent predictor of MACE after multivariate adjustment (hazard ratio 3.42 (confidence interval 1.45-8.08), p<0.01) with no significant difference in the area at risk, infarct size, myocardial salvage index, extent of microvascular obstruction, and left ventricular ejection fraction [6].

Ischemic cell death during MI leads to a multiphase reparative response in which the damaged tissue is replaced with a fibrotic scar produced by fibroblasts and myofibroblasts. This also induces geometrical, biomechanical, and biochemical changes in the uninjured ventricular wall eliciting a reactive remodeling process that includes interstitial and perivascular fibrosis [7]. Although the initial reparative fibrosis is crucial for preventing rupture of the ventricular wall, an exaggerated fibrotic response and reactive fibrosis outside the injured area are detrimental as they lead to progressive impairment of cardiac function and eventually to heart failure [7].

The extracellular matrix (ECM) is a dynamic microenvironment and a major contributor to the adverse ventricular remodelling that follows MI, via activation of both direct pro-fibrotic pathways and matrix metalloproteinases (MMPs) and fibronectin (Fn) that enhance collagenase activity. Reactive fibrosis, i.e. deposition of ECM materials remote from the region of MI is clearly detrimental to ventricular function and contributory to adverse outcomes of post-MI [8]. Therefore, reversal of this process is an important therapeutic target in post-MI management.

Quercetin as one of flavonoids has long been acknowledged for its unique antioxidant properties; it possesses other activities that may be relevant to heart ischemia–reperfusion. It may prevent production of oxidants (e.g. by inhibition of xanthine oxidase and chelation of transition metals), inhibit oxidants from attacking cellular targets (e.g. by electron donation and scavenging activities), block propagation of oxidative reactions (by chain-breaking antioxidant activity), and reinforce cellular antioxidant capacity (through sparing effects on other antioxidants and inducing expression of endogenous antioxidants) [9]. Flavonoids also possess anti-inflammatory and anti-platelet aggregation effects through inhibiting relevant enzymes and signaling pathways, resulting ultimately in lower oxidant production and better re-establishment of blood in the ischemic zone [9].

The objective of the research was to investigate potential antifibrotic effects of Quercetin in patients with acute MI and AH.

Materials and methods

130 patients with ST-elevation MI were involved in the study. There were 82 (63.07%) males and 48 (36.93%) females. The average age was (64.68±12.59) years. All the patients were divided into 2 groups: 63 persons with AH and 67 persons without AH. Each group was divided into 2 subgroups according to the therapeutic scheme: subgroup IA included 33 patients receiving basic treatment; subgroup IB included 34 patients who additionally received Quercetin (parenterally within the first 5 days, and, then, orally at a dose of 40 mg twice a day); subgroup IIA involved 33 patients receiving basic treatment; subgroup IIB comprised 30 patients who additionally received Quercetin at similar doses.

Transthoracal echocardiography was performed and the types of myocardial remodeling were calculated according to the recommendations of the American Society of Echocardiography (ASE) and the European Association of Echocardiography [10].

Plasma levels of Fn and matrix metalloproteinase 9 (MMP-9) were detected using the ELISA method.

The investigation was performed before, on the 7th and the 28th days of treatment as well as 3 months after treatment.

The study was performed in accordance with the Helsinki Declaration and Good Clinical Practice Guidelines. The study was approved by the local ethics committee and written informed consent was obtained from all the patients.

Categorical variables are presented as percentages, whereas normally distributed continuous variables are presented as the mean (M) and the standard error of the mean (m) and non-normally distributed ones are presented as the median and the interquartile range (Me (IQR)). Categorical variables were compared by the $\chi 2$ test and continuous variables were compared using the t-test or the Mann-Whitney U test. A p value of <0.05 was considered statistically significant. All tests were 2-sided. The analyses were performed using Statistica software (version 12.0).

Results and discussion

In all the patients, a significant decrease in Fn plasma levels was observed since the 28th day of treatment; however, it was more significant in group of additional prescription of Quercetin (Table 1). In subgroup IA, this parameter decreased by 21.12% (p<0.01), and by 43.35% (p<0.001) at the end of the study. In patients of subgroup IB, Fn plasma level decreased by 33.57% (p<0.01) since the 28th day of treatment and by 51.70% (p<0.01) at the end of the 3rd month being 15.15% and 14.1% higher (p<0.05) than in patients receiving basic treatment.

Similar dynamic was observed in patients with MI and AH. In patients of subgroup IIA, Fn plasma level decreased by 20.79% (p<0.01) on the 28th day of study, and by 39.13% (p<0.001) at the end of the observation period. We noted slower dynamics of this parameter in patients with AH (Δ=9.72%, p<0.05). Additional prescription of Quercetin resulted in more intensive reduction in Fn plasma level: by 25.34% (p<0.01) on the 28th day of treatment and by 47.99% (p<0.01) at the end of study being 9.72% and 8.3% higher (p<0.05) than in patients receiving basic treatment.

Revascularization and pharmacological management of MI resulted in the reduction in MMP-9 plasma levels in all the patients since the 7th day of treatment; however, it was more significant in group of additional prescription of Quercetin (Table 1). In subgroup IA, this parameter decreased by 11.59% (p<0.05) on the 7th day of treatment, by17.48% (p<0.01) on the 28th day and by 24.63% (p<0.001) on the 3rd month. In subgroup IB, it decreased by 14.52% (p<0.05), 34.57% (p<0.01) and 37.31% (p<0.001), respectively, being 19.03% and 15.04% higher (p<0.05) than in patients receiving basic treatment (since the 28th day until the 3rd month).

During the observation periods, in patients with concomitant AH, plasma levels of MMP-9 decreased by 12.69% (p<0.05), 20.77% (p<0.01) and 24.29% (p<0.001), respectively. In group of additional prescription of Quercetin, this parameter decreased by 15.19% (p<0.05), 34.43% (p<0.01) and 38.05% (p<0.001), respectively.

According to last clinical trials, an ideal therapy for MI-induced cardiac injury would combine the inhibition of reactive fibrosis (and other remodeling processes) in non-infarcted areas with the induction of the regeneration of the infarcted myocardium for example, by direct reprogramming of fibroblasts to cardiomyocytes. A more detailed understanding of the gene programmes, signaling cascades, and cellular metabolic routes deciding between regeneration in neonatal rodents or scarring and remodeling in adults is, however, critical for the development of such therapeutics [7].

Conclusions

Quercetin possesses potential antifibrotic properties causing a reduction in plasma levels of Fn and MMP-9 in patients with

Table 1. Dynamics of fibrosis markers in patients with MI

Parameter	Patients without AH, n=67		Patients with AH, n=63	
	IA, n=33	IB, n=34	IIA, n=33	IIB, n=30
Fibronectin, mcg/ml				
-before treatment	479.87±15.41	483.56±17.11	494.74±16.11	489.77±17.11
-on the 7th day	471.43±14.11	476.21±14.47	483.47±17.14	481.57±14.54
-on the 28th day	378.54±16.14°°	321.21±13.47°°°*	391.87±15.47°°	365.68±13.74°°*#
-on the 3rd month	271.87±15.61°°°	233.56±12.87°°°*	301.14±13.47°°°#	254.71±19.11°°°*
MMP-9, ng/ml				
-before treatment	91.78±6.98	93.74±5.87	97.89±5.79	98.74±6.32
-on the 7th day	81.14±4.23°	80.13±6.11°	85.47±4.78°	83.74±5.11°
-on the 28th day	75.74±5.14°°	61.33±5.77°°*	77.56±6.11°	64.74±4.98°°*
-on the 3rd month	69.17±7.11°°	58.77±4.78°°°*	74.11±5.11°°	61.17±5.74°°°*

Notes:

1. Continuous variables are presented as the mean (M) and the standard error of the mean (m);
2. Difference between parameters: ° p<0,05; °° p<0,01; °°° p<0,001 – in one group compared to preliminary data;
3. Difference between parameters: # p<0,05 depending on concomitant AH;
4. Difference between parameters: * p<0,05; ** p<0,01; *** p<0,001 – compared to group of basic treatment

MI and concomitant AH.

Prospects for further research include the study of different effects of Querecetin on the regression of left ventricular remodeling after MI.

Conflict of interests: none

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