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CORRECTION OF INFLAMMATION SIGNS IN POSTMENOPAUSAL WOMEN WITH THE METABOLIC SYNDROME

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Key words: metabolic syndrome; menopause; treatment; inflammation

The metabolic syndrome is a common condition that predisposes individuals to the risk of developing cardiovascular diseases and type 2 diabetes. Menopause is known to be associated with a fall in the estrogen levels accompanied with many health changes. Changes in the hormone levels in menopause, in particular estrogen deficiency are associated with increase in the body fat. Additionally, it sounds an alarm for women's health since it leads to elevated blood pressure, insulin resistance and dyslipidemia. These changes may contribute to increased risks of the metabolic syndrome (MetS) in menopause women. Obesity shares the presence of an inflammatory component with most chronic diseases, it accounts for development of the metabolic disease and other associated health alterations. The aim of the study was to study the effect of bioflavonoid Quercetin and ω -3 PUFA on some components of inflammation in menopausal women with MetS. Material and methods. Eighty menopausal women with MetS were observed. All participants were divided into four groups: group I – basic therapy (20 patients); group II (19 patients) – basic therapy + Quercetin; group III (21 patients) – basic therapy + ω -3 PUFA; group IV (20 patients) – basic therapy + ω -3 PUFA + Quercetin. The general white blood count in the blood and their subpopulations has been determined; the leukocytal indexes and the degree of endogenous intoxication have been calculated by the erythrocytes sorptivity (ES) test. Results. The use of Quercetin has shown the most significant results for dynamics of white blood cells count, its subpopulations in the blood, leukocytal indexes and the degree of endogenous intoxication. Conclusions. Thus, the additional use of Quercetin has a strong influence on the components of chronic inflammation in the metabolic syndrome in menopausal women.

The metabolic syndrome, also known as Syndrome X, Insulin Resistance Syndrome or Dysmetabolic Syndrome, is a common condition that predisposes individuals to the risk of developing cardiovascular diseases and type II diabetes. The syndrome is the complex of risk factors such as central obesity, high blood pressure, hyperglycaemia, impaired glucose tolerance, hypertriglyceridaemia, as well as the low level of high density lipoprotein cholesterol in the blood plasma [7, 9]. It is known that about 20-25 per cent of the world's population have the metabolic syndrome and are three times more likely to die from heart attack or stroke compared to people without the syndrome [2-4]. The risk of cardiovascular diseases associated with the metabolic syndrome seems to be particularly high in women; half of all cardiovascular events in women is connected with the metabolic syndrome [5, 8].

Menopause is an important physiological event, with cessation of menstruation indicating the end of the woman's reproductive age [7, 10]. Menopause is associated with a fall in the estrogen levels accompanied with many health changes. Changes in the hormone levels in menopause, in particular estrogen deficiency are associated with increase in the body fat. Additionally, it sounds an alarm for women's health since it leads to elevated blood pressure, insulin resistance and dyslipidemia [9]. These changes may contribute to increased risks of the metabolic syndrome (MetS) in menopause women.

Obesity shares the presence of an inflammatory component with most chronic diseases, it accounts for development of the metabolic disease and other associated health alterations. This inflammatory state is reflected in increased circulating levels of pro-inflammatory proteins, and it occurs not only in adults, but also in adolescents and children [11]. The chronic inflammatory response has its origin in the links existing between the adipose tissue and the immune system.

Nowadays there are some experimental and clinical trials of natural compounds, bioflavonoids and ω -3 polyunsaturated fatty acids (PUFA) used for management of MetS, but their influence on inflammation during menopause is unclear [6].

The aim of the study was to study the effect of bioflavonoid Quercetin and ω -3 PUFA on some components of inflammation in menopausal women with MetS.

Materials and Methods

Eighty menopausal women with MetS were observed. All participants were randomly divided into four groups: group I – basic therapy (20 patients); group II (19 patients) – basic therapy + Quercetin ("Quertin" manufactured by SIC "Borshchahivskiy Chemical and Pharmaceutical plant" PJSC, Ukraine; approved by the Order of MPH of Ukraine No. 649(2) from 12.04.2011, the registration certificate UA/0119/02/01) – 40 mg twice a day 30 min before meals; group III (21 patients) – basic therapy + ω -3 PUFA ("Omacor" manufactured by

Table 1

Dynamics of leukogram values in the patients under research (M±m)

Value	Groups of observation			
	I, n=20	II, n=19	III, n=21	IV, n=20
White blood cells, G/l				
Before treatment	6.83±0.21	6.98±0.27	7.01±0.25	6.99±0.26
After treatment	6.84±0.23 ⁴	6.24±0.21 ¹	6.99±0.23 ⁴	6.20±0.24 ¹
Lymphocytes, G/l				
Before treatment	1.86±0.07	1.98±0.09	1.97±0.08	1.95±0.07
After treatment	1.87±0.09 ⁴	1.67±0.07 ²	1.96±0.06 ⁴	1.64±0.07 ²
Monocytes, G/l				
Before treatment	0.39±0.03	0.37±0.06	0.38±0.05	0.39±0.06
After treatment	0.38±0.06 ⁴	0.36±0.07 ⁴	0.37±0.06 ⁴	0.38±0.07 ⁴
Neutrophils, G/l				
Before treatment	4.44±0.11	4.54±0.13	4.63±0.12	4.55±0.11
After treatment	4.45±0.13 ⁴	4.01±0.14 ²	4.61±0.15 ⁴	3.99±0.13 ³

Notes: 1. ¹ Significance of differences between values before and after treatment $p < 0.05$; 2. ² Significance of differences between values before and after treatment $p < 0.01$; 3. ³ Significance of differences between values before and after treatment $p < 0.001$; 4. ⁴ Significance of differences between values before and after treatment $p > 0.05$.

“Solvay Pharmaceuticals GmbH”, Germany; approved by the Order of MPH of Ukraine No. 924 from 07.12.2010, the registration certificate UA/2108/01/01) – 1 capsule (1000 mg) once a day; group IV (20 patients) – basic therapy + ω -3 PUFA + Quercetin – in the doses given above. The basic therapy included the life style modification and drug therapy. The basic drug therapy included the treatment of arterial hypertension (ESC, 2013): RAAS blocker (ACE-inhibitor or AR II-blocker) in individual doses. In case of non-achievement of the target levels of hypertension the calcium channel blockers were prescribed additionally. High-risk or very high-risk patients additionally received acetylsalicylic acid (75 mg per day) and Rosuvastatin (10 mg per day). Correction of glucose metabolism was performed according to the recommendation of the European Society of Cardiology (2013) and the International Diabetes Federation (2012). All patients with MetS were examined prior their treatment and in 6 weeks. The general white blood count in the blood and their subpopulations was

determined; the leukocytal indexes were calculated. The degree of endogenous intoxication was determined by the erythrocytes sorptivity (ES) test [1]. All results were processed statistically by Statistika 6 programme.

Results and Discussion

The additional use of Quercetin led to reduction in the leukocyte count in the peripheral blood of the patients with MetS (Tab. 1). Thus, women in group II showed decrease of this indicator by 11.9% compared to the control group ($p < 0.05$); and in group IV – by 12.7% ($p < 0.05$). In contrast, the baseline treatment and additional administration of ω -3 PUFAs did not show the reliable dynamics for the leukocyte count ($p > 0.05$). The analysis of leukocyte subpopulations also showed a positive effect of Quercetin on the absolute number of lymphocytes and neutrophils. In particular, the lymphocyte count in group II decreased by 18.6% ($p < 0.01$); in group IV – by 18.9% ($p < 0.01$). However, in group I and III no significant changes were observed ($p > 0.05$). Similarly, Quercetin contributed to normalization of the neutrophil count:

Table 2

Dynamics of leukocytal indexes in the patients under research (M±m)

Value	Groups of observation			
	I, n=20	II, n=19	III, n=21	IV, n=20
INMR				
Before treatment	11.38±0.61	12.27±0.71	12.18±0.69	13.67±0.68
After treatment	11.71±0.62 ⁴	11.14±0.59 ²	12.46±0.57 ⁴	11.45±0.71 ²
ILMR				
Before treatment	4.97±0.43	5.64±0.39	5.62±0.38	5.92±0.37
After treatment	4.92±0.38 ¹	4.64±0.38 ³	5.52±0.37 ²	4.31±0.38 ³
IN/MC				
Before treatment	2.06±0.11	2.03±0.09	2.07±0.09	2.04±0.08
After treatment	2.08±0.09 ⁴	2.08±0.08 ¹	2.08±0.11 ⁴	2.09±0.12 ¹

Notes: 1. ¹ Significance of differences between values before and after treatment $p < 0.05$; 2. ² Significance of differences between values before and after treatment $p < 0.01$; 3. ³ Significance of differences between values before and after treatment $p < 0.001$; 4. ⁴ Significance of differences between values before and after treatment $p > 0.05$.

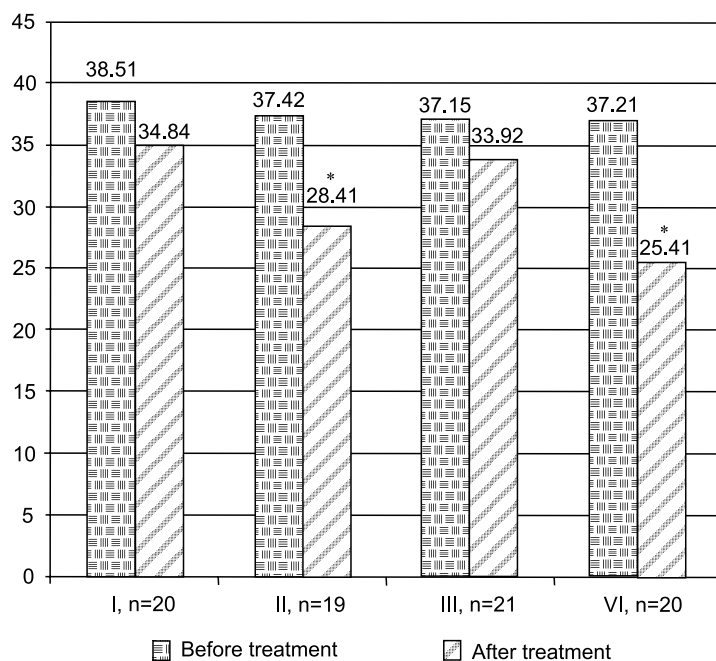


Fig. Dynamics of the ES index in patients under research (in %).
Note: * – Significance of differences between values before and after treatment $p < 0.01$.

in group II by 13.2%, and in group IV – by 14.1% ($p < 0.001$). The basic therapy and additional administration of ω -3 PUFA did not influence on this index ($p > 0.05$). None of the treatment regimens used had no significant effect on the number of peripheral blood monocytes in menopausal women with MetS.

According to the dynamics of the leukogram values the leukocytal indexes also changed (Tab. 2). Significant changes of the index of neutrophils to monocytes ratio (INMR) occurred in the group of women with MetS treated by Quercetin alone or in combination with ω -3 PUFA. Thus, INMR decreased by 10.1% in group II, and by 19.4% – in group IV ($p < 0.01$). However, the basic therapy or its combination with ω -3 PUFA had no effect on this indicator ($p > 0.05$). The index of lymphocytes to monocytes ratio (ILMR) significantly decreased in all groups under research, but dynamics was more expressed when using Quercetin and its combination with ω -3 PUFA: in patients of group I this index decreased by 10% ($p < 0.05$); in group II – by 21.5% ($p < 0.001$); in group III – by 20% ($p < 0.05$); in group IV – by 37.4% ($p < 0.001$). The index of the ratio of neutrophils to mononuclear cells (IN/MC) was changed only

during administration of Quercetin alone or in its combination with PUFA by 1.02 times ($p < 0.05$). Dynamics of IN/MC in groups of the baseline treatment and additional use of ω -3 PUFAs were insignificant ($p > 0.05$).

In our opinion, the effect of Quercetin on the leukocyte count in the peripheral blood and their subpopulations are associated with the anti-inflammatory effect of this bioflavonoid implemented via numerous mechanisms.

Due to its anti-inflammatory and antioxidant effects Quercetin probably had a pronounced effect on dynamics of the ES index as a marker of endogenous intoxication (Fig.). Thus, in patients of group II it decreased by 1.32 times ($p < 0.01$); in group IV – by 1.46 times ($p < 0.01$). The basic therapy or its combination with ω -3 PUFA showed no significant effect on the value of ES ($p > 0.05$).

CONCLUSIONS

Thus, the additional use of Quercetin has a strong influence on the components of chronic inflammation in the metabolic syndrome in menopausal women.

The perspectives of further investigations are the study of the effect of Quercetin and PUFA on the immune system values of I and II degree.

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КОРЕКЦІЯ ПРОЯВІВ ЗАПАЛЕННЯ У ЖІНОК ПОСТМЕНОПАУЗАЛЬНОГО ПЕРІОДУ ІЗ МЕТАБОЛІЧНИМ СИНДРОМОМ

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Ключові слова: метаболічний синдром; запалення; менопауза; лікування

Метаболічний синдром – частий стан, який підвищує ризик виникнення серцево-судинних захворювань та цукрового діабету II типу. Відомо, що метаболічний синдром у жінок частіше трапляється в менопаузі. Вивчається роль запалення при метаболічному синдромі. Мета роботи полягала у вивченні впливу біофлавоноїду кверцетину та препаратів ω -3 ПНЖК на окремі компоненти запалення у жінок у менопаузі з МС. Обстежено 80 жінок у постменопаузі з метаболічним синдромом, які були розподілені на чотири групи: базове лікування, базове лікування та кверцетин, базове лікування та ω -3 ПНЖК, базове лікування з кверцетином та ω -3 ПНЖК. Досліджена кількість лейкоцитів периферійної крові, абсолютне число їх субпопуляцій, лейкоцитарні індекси, ступінь ендогенної інтоксикації за тестом сорбційної здатності еритроцитів; відмічений виразний позитивний вплив кверцетину на кількість лейкоцитів у крові обстежених жінок та на окремі субпопуляції, лейкоцитарні індекси та сорбційну здатність еритроцитів. Зроблений висновок, що додаткове призначення кверцетину чинить більш виразний вплив на компоненти хронічного запалення при МС у жінок у менопаузі.

КОРЕКЦИЯ ПРОЯВЛЕНИЙ ВОСПАЛЕНИЯ У ЖЕНЩИН ПОСТМЕНОПАУЗАЛЬНОГО ПЕРИОДА С МЕТАБОЛИЧЕСКИМ СИНДРОМОМ

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Ключевые слова: метаболический синдром; воспаление; лечение; менопауза

Метаболический синдром – частое состояние, которое повышает риск возникновения сердечно-сосудистых заболеваний и сахарного диабета II типа. Известно, что метаболический синдром (МС) чаще развивается во время менопаузы. Изучена роль воспаления при МС. Целью работы было изучение влияния биофлавоноида кверцетина и препаратов ω -3 ПНЖК на определенные компоненты воспаления у женщин с МС в менопаузе. Обследованы 80 женщин в постменопаузе с МС, которые были разделены на четыре группы: базовое лечение, базовое лечение и кверцетин, базовое лечение и ω -3 ПНЖК, базовое лечение и комбинация кверцетина с ω -3 ПНЖК. Определено количество лейкоцитов в крови, их субпопуляции, рассчитаны лейкоцитарные индексы и степень эндогенной интоксикации за тестом сорбционной способности эритроцитов. Отмечено выраженное положительное влияние кверцетина на количество лейкоцитов, определенные их популяции и лейкоцитарные индексы; определена степень сорбционной способности эритроцитов. Сделан вывод, что дополнительное назначение кверцетина обуславливает более выраженное влияние на компоненты хронического воспаления при МС в менопаузальных женщин.