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The Effects of Quercetin on Proinflammatory Cytokine's Levels in Postmenopausal Women with Metabolic Syndrome

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Metabolic syndrome (MetS) is becoming a worldwide epidemic as a result of the increased prevalence of obesity and a sedentary lifestyle, and the prevalence of MetS in the adult population is relatively high. Many studies showed the high prevalence of metabolic syndrome among postmenopausal women. The purpose of our study was to investigate of quercetine' influence on proinflammatory cytokines level in blood of postmenopausal women with MetS. The 39 postmenopausal women with MetS were referred to the study, and divided into 2 groups: 1-st – control group (patients with MetS which treated by basic medication: RAAS blockers, acetylsalicylic acid and statin); 2-nd – additionally used quercetine in dose 40 mg twice a day 30 min before meals. Quercetine is strong antiinflammation medicine which decreases IL-1β, IL-6, Ltr B_4 levels in blood serum.

Keyword: Metabolic Syndrome, Menopause, Cytokine

1. Introduction

Metabolic syndrome (MetS) is a common condition that predisposes individuals to the risk of developing cardiovascular diseases and type 2 diabetes. The syndrome is the assemblage of risk factors such as central obesity, high blood pressure, hyperglycaemia, impaired glucose tolerance, hypertriglyceridaemia as well as low levels of high density lipoprotein cholesterol[1]. It is estimated that about 20–25 percent of the world's population have the metabolic syndrome and are three times more likely to die from heart attack or stroke compared with people without the syndrome[2]. The risk of cardiovascular diseases assigned to metabolic syndrome seems to be particularly high in women with the estimation that half of all cardiovascular events in women are linked to metabolic syndrome[3]. Amongst pre-and postmenopausal women it ranges from 13.8% to more than 60.0%[4].

The etiology of the syndrome is not clearly defined, but it is linked with visceral obesity[5]. Hence, the theory of metabolic changes in postmenopause and increased abdominal obesity as a result of decrease in estrogen production is one of the hypotheses that is used to explain the increased incidence of the syndrome during this period[6]. Adipose tissue is the key endocrine organ with autocrine regulation. It plays a central role in obesity-associated complications, such as type 2 diabetes, dyslipidemia, insulin resistance, coronary artery disease, low-grade chronic inflammation etc. It's now established that adipose tissue comprises near 50% adipocytes and near 50% other cells (pre-adipocytes, vascular, neural and immune cells and leukocytes)[7]. The adipocytes, pre-adipocytes and

macrophages secrete a wide range of hormones and cytokines, which take place in inflammation[7].

Quercetin is categorized as a favonol, one of the six subclasses of favonoid compounds. Flavonols are present in a wide variety of fruits and vegetables. Quercetin appears to have many potential benefcial efects on human health. In some instances (e.g. blood pressure lowering) clinical studies have been conducted. In other areas (e.g. cancer) all or most of the current research is pre-clinical.

The purpose of our study was to investigate of quercetine' influence on proinflammatory cytokines level in blood of postmenopausal women with MetS.

2. Materials and Methods

This cross-sectional study was performed in the Central Municipal Hospital of Ivano-Frankivsk, Ukraine (West part of Ukraine). The 39 postmenopausal women with MetS were referred to the study. Postmenopausal women who had at least 1-year history of cessation of menses were included. Postmenopausal women were considered to have metabolic syndrome if they had any three or more of the clinical criteria (IDF – International Diabetes Federation, AHA – American Heart Association and NHLBI – National Heart, Lung and Blood Institute, 2009 guideline). All the included subjects provided an informed consent. All observed patients were divided into 2 groups: 1-st – control group (patients with MetS which treated by basic medication: RAAS blockers, acetylsalicylic acid and statin); 2-nd – additionally used quercetine in dose 40 mg twice a day 30 min before meals.

Interleukin 1β (IL-1β), interleukin 6 (IL-6), and leukotriene B4 (Ltr B_4) levels in blood serum were determined using commercial ELISA kits (ProCon, Russia, Cytimmune Sciences Inc., USA; Amersham Pharmacia Biotech, UK) according to the manufacturer's instructions. Statistical analyses were performed using the Statistica 6.1 (StatSoft, Tulsa, OK, USA). Statistical significance was assumed at $p<0.05$.

3. Results of Study and Discussion

The dynamics of IL-1β levels in blood serum during management of MetS were statistical significant in all groups (see table). But more strong decrease of this cytokine level was in 2-nd group: for 52,34% (from 59,78±3,15 pg/ml to 39,24±3,19 pg/ml) ($p<0,001$). In first group the IL-1β level decreased only for 22,6% (from 55,75±3,11 pg/ml to 45,47±3,45 pg/ml) ($p<0,01$).

Similar dynamics also was observed for IL-6: for 23,0% (from 14,20±1,08 pg/ml to 11,54±1,06 pg/ml) ($p<0,05$) – in first group; for 60,8% (from 16,32±1,09 pg/ml to 10,15±1,08 pg/ml) ($p<0,001$) – in group with additional use of quercetin.

Table: The dynamics of serum cytokines and Ltr B_4 levels during management of menopausal MetS (M±m)

Parameters	Observation' groups	
	I, n=20	II, n=19
IL-1β, pg/ml Before treatment After treatment	 55,75±3,11 45,47±3,45[2]	 59,78±3,15 39,24±3,19[2]
IL-6, pg/ml Before treatment After treatment	 14,20±1,08 11,54±1,06[1]	 16,32±1,09 10,15±1,08[3]
Ltr B_4, pg/ml Before treatment After treatment	 61,34±3,18 56,54±3,12[1]	 62,49±3,15 39,81±3,12[3]

Remarks:

1. Difference between parameters before and after treatment $p<0,05$;
2. Difference between parameters before and after treatment $p<0,01$;
3. Difference between parameters before and after treatment $p<0,001$;
4. Difference between parameters before and after treatment $p>0,05$.

Basic therapy caused decrease of Ltr B_4 serum levels only for 8,5% (from 61,34±3,18 pg/ml to 56,54±3, pg/ml) ($p<0,05$). However in 2-nd group – for 56,9% (from 62,49±3,15 pg/ml to 39,81±3,12 pg/ml) ($p<0,001$).

Several epidemiological studies have reported an inverse association between quercetin intakes and coronary heart disease. In the Zutphen Elderly Study, the risk of heart disease mortality decreased signifcantly as favonoid intake increased, with the favonoid-containing foods most commonly eaten in this study containing high amounts of quercetin compounds (e.g. tea, onions, apples)[8]. In a cohort of the same study, dietary favonoids (mainly quercetin) were inversely associated with stroke incidence. In the Finnish Mobile Clinic Health Examination Survey, low favonoid intake was associated with higher risks of coronary disease. Intakes of onions and apples, the main dietary sources of favonoids as well as rich sources of quercetin compounds, had similar associations[9].

Human studies have been mixed as to whether quercetin has anti-infammatory efects. Two weeks of quercetin supplementation in healthy subjects at doses up to 150 mg/day did not afect TNF-a. Tis lack of efect occurred despite a signifcant increase in plasma quercetin levels[10]. A dose of 1,000 mg/day quercetin for six weeks failed to prevent exercise-induced increases in C-reactive protein (CRP) in 40 athletes[11]. In a study of overweight and obese subjects with metabolic syndrome traits, quercetin (150 mg/day) had no efect on TNF-a or CRP when compared with placebo[12]. In a similar study, quercetin (150 mg/day) for six weeks had no efect on CRP, but TNF-a was decreased[13].

However, in vitro, quercetin inhibits production of infammation-producing enzymes (cyclooxygenase [COX] and lipoxygenase [LOX]) and some of their metabolites[14].

4. Conclusion

Thus, quercetine is strong anti inflammation medicine which can be used for treatment low-grade inflammation at MetS.

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