ISSN: 2277- 7695
CODEN Code: PIHNBQ
ZDB-Number: 2663038-2
IC Journal No: 7725

Received: 21-11-2013
Accepted: 11-01-2014

Vol. 2 No. 12. 2014
Online Available at www.thepharmajournal.com

THE PHARMA INNOVATION - JOURNAL

Correction of lipid and purine metabolism in patients with arterial hypertension, obesity and gout

Maryana Vatseba*

1. SHEI "Ivano-Frankivsk National Medical University", The department of Internal Medicine №2 and Nursing (Head of the Faculty – Doctor of the Medical Science, Professor Vakaliuk I.P.)
[E-mail: vatseba@yandex.ru; Tel: 0506983879]

Our study aimed to evaluate the methods of correction of lipid and purine metabolism in patients with hypertension combined with obesity and gout. The study involved 46 patients with hypertension, gout and obesity. The aim of research was to improve treatment of patients with hypertension, gout and obesity by using Losartan and Meldonium. Application to the basic therapy Losartan and Meldonium improves lipid profile and reduces the level of uric acid. Thus, the combined use of Losartan and Meldonium is feasible, effective and safe for prolonged use.

Keyword: Species of the genus Geranium L., Volatile compound, Chromatographymass-spectrometry method, Leaf anatomy.

1. Introduction

Arterial hypertension (AH) is one of the major cardiovascular diseases, which greatly contributes to the growth of the mortality of the European population by increasing the risk of the development of the serious cardiovascular complications. AH, ischemic heart disease (IHD), obesity, hyperuricemia (HU) are the pathologic states, that became pandemic in the modern world [1]. The causes of the increase in the frequency of the cardiovascular pathology are the following negative phenomena: sedentary lifestyle, chronic stress, growth of the caloric values of the food products, extra weight and obesity [6]. It was proved, that the incidence of ischemic heart disease and AH is higher in patients with gout, than in common people. Besides most of these patients have at least 2 cardiovascular risk factors, which is worse than having one cardiovascular risk factor or none [5]. Studying the gout disorder in the last century showed that it is a metabolic disease, in which the misbalance of one of the metabolic components causes the cascade of the pathologic genetic reactions, and, thus, leads to the change of the other components of the metabolic exchange. The incidence of gout significantly increased in the last 10 years. In the developed countries at least 1-3% of the adult population (mostly men) is diagnosed with gout. In Ukraine the incidence of gout is 5-28 cases out of 1000 of men, and 1-6 cases out of 1000 of women [2, 3, 7]. The interrelations between the extra weight, incidence of HU and development of the coronary diseases were proved [2]. The patients with gout have a high incidence of obesity. AH, which according to different data is found in 25-50% of the patients diagnosed with gout, does not depend on the length of the gout disease and is associated with a bad prognosis in these patients [6]. It was established, that the interrelation between the elevated level of the uric acid (UA) and the development of the cardiovascular diseases (CVD) is done through the affection of the target organs, but up till now there is no research study, describing the role of the UA in the development of the CVD [3, 8].

2. The purpose of the Study

To evaluate the methods of correction of lipid and purine metabolism in patients with hypertension combined with obesity and gout.

3. Methods of Research

We examined 46 men with the diagnosis of essential AH of the second degree with concomitant IHD, obesity of the 1-2 degrees and gout. The average age of these men was 63.2 ± 1.8 years. All patients were randomly divided into 4 groups. First group included 12 patients, who were receiving basic therapy (BT). The second group also included 11 patients, who besides basic therapy were receiving the blocker of the receptors of the 1st type angiotensin II Losartan (Lorista) (L), prescribed at a dose of 50-100 mg per day. Third group included 12 patients, who besides basic therapy were receiving 5 ml of the 10% solution of Meldonium digidratum (Metamax) (M) in the 20 ml of sodium chloride solution by intravenous injection during 10 days with the following switch to the oral form of the medication (250 mg twice a day during 1 month). The fourth group included 11 patients, who besides basic therapy were taking Meldonium digidratum (Metamax) (M) and angiotensin receptor blocker II Losartan (Lorista) (L). Verification of the diagnosis, determination of the stage and degree of hypertension was conducted according to the criteria recommended in 2013 by the European Society of arterial hypertension (European Society of Hypertension - ESH) and European Society of Cardiology (European Society of Cardiology - ESC) (Mancia G. Et al. , 2007). The diagnosis of gout was set according to the criteria of S. L. Wallace, recommended by the World Health Organization (2002) and EULAR (2013).

The presence and degree of obesity was estimated by the formula:

$$BMI\ (kg/m2) = weight\ (kg) / height\ (m2).$$

The study included: body mass index (BMI). Biochemical studies included the determination of total cholesterol (TC), triglycerides (TG), High density lipoprotein (HDL) using enzymatic methods with the reagents of the company Filisit diagnosis and uric acid – using colorimetric method with the reagents of the company Filisit diagnostics. The level of Low density lipoprotein (LDL) in the blood was calculated using the mathematical formula: LDL cholesterol = total cholesterol - (HDL + TG / 2.2) mmol / l. Calculated also atherogenic factor (AF) as follows: AF = (cholesterol - HDL cholesterol) / HDL. Statistic calculations of the data was done by using the computer program STATISTIKA-8 and the package of the statistic functions of the program «Microsoft Excel». We determined the mean arithmetic value M, mean square deviation δ, average error of the mean arithmetic value M, the number of the variant (n), the likelihood of the difference between 2 mean arithmetic "p"s, paired t-test.

4. The Results of the Study

Almost in 90% of patients, increased levels of total cholesterol (TC), low-density lipoprotein (LDL), triglycerides (TG) and high-density lipoprotein (HDL) reduction was found (Table 1). It was established that the basic therapy identifies the weakest positive effect. The level of TC decreased by 7.26% ($p < 0.05$) in the 1-st group, by 7.64% ($p < 0.05$) in the 2 and by 10.0% ($p < 0.05$) in the 3rd. The most marked reduction of total cholesterol (12.4%, $P < 0.05$) noted in patients after after the combined treatment with BT, L and M. The level of LDL after the treatment with BT decreased by 6.8 % ($p<0.05$), following the treatment with BT and L it decreased by 6.6 % ($p<0.05$) and after the combined treatment with BT and M decreased by 5.5% ($p<0.05$). The largest decrease of LDL (7.2%, $p < 0.05$) was observed using BT, L and M. With usage of the BT the level of TG was significantly decreased by 11.4% ($p < 0.05$), BT and L - 14.7% ($p < 0.05$), BTand M - 14.0% ($p < 0.05$), BT, L and M 16, 7% ($p < 0.05$). Increasing the level of HDL was the highest in the 4 group - its level increased by 5.4%, in patients in the 1st, 2nd and 3rd groups - it has increased by only 2.6% ($p < 0.05$). Increased

levels of uric acid was noted in all groups. With usage of the BT the decrease of the uric acid was not seen. The best effect was achieved in the 2nd and 4th groups. With usage of the BT and L uric acid decreased by 31.3% (p <0.05), after the treatment with BT and M by24.8% (p <0.05), and after BT, L and M combined therapy by 40 6% (p <0.05). So, it should be noted that the combination of BT, L and M has a positive effect on lipid and purine metabolism. Best positive effect this combined therapy has on reduction of uric acid, cholesterol, triglycerides and increases the level of HDL.

Table 1: Dynamics of the indicators of purine and lipid metabolism after the performed treatment in patients diagnosed with AH, concomitant with obesity and gout (absolute value Δ%), M±m.

№ п/п		I group n=12	II group n=11	III group n=12	IV group n=11
TC, mmol / L	Before treatment	5,92±0,35	6,15±0,26	6,0+0,24	6,2+0,35
	After treatment	5,49+0,26 >0,05 -7,26	5,68+0,18 -7,64	5,4+0,11* -10	5,43+0,17* -12,4
TG, mmol / L	Before treatment	2,1±0,25	2,58±0,34	2,2±0,14	2,27±0,32
	After treatment	1,86±0,32 -11,4	2,2±0,26 -14,7	1,89±0,23* -14,0	1,89±0,33* -16,7
HDL, mmol /L	Before treatment	1,13±0,05	1,15±0,03	1,13±0,05	1,11±0,05
	After treatment	1,16±0,02 +2,6	1,18±0,01 +2,6	1,16±0,03 +2,6	1,17±0,05 +5,4
LDL, mmol / L	Before treatment	3,92±0,23	4,03±0,26	3,99±0,29	3,98±0,35
	After treatment	3,65±0,21 -6,8	3,76±0,23 -6,6	3,77±0,22 -5,5	3,69±0,32 -7,1
AF, cu	Before treatment	4,23±0,27	4,33±0,28	4,32±0,24	4,5±0,24
	After treatment	3,73±0,23 -11,3	3,83±0,21 -11,5	3,65±0,3 -15,5	3,78 ±0,34 -16
Uric acid, mkmol / L	Before treatment	585,16±29,0	532,1±42,7	571,0±28,8	593,2±30,0
	After treatment	430,23±24,5 -26,4	365,5±32,2* -31,3	429,2±24,7 -24,8	352,1±32,1* -40,6

Notes: Δ% - difference of the index in comparison with values before treatment; p – validity of the data difference in comparison with values before treatment*- p>0.05.

5. Conclusions:

1. For the appointment of timely diagnostics and adequate treatment for all patients with hypertension combined with obesity and gout, the study of lipid and purine metabolism must be added to the complex of survey.
2. In the case of pathological changes of lipidogram and purine metabolism, in patients with hypertension combined with obesity and gout, additional lipid-lowering and uric acid lowering therapy should be given for the correction of this changes.
3. Losartan is an effective and safe antihypertensive medication for the treatment of the patients diagnosed with AH, concomitant with obesity and gout. It has a

positive effect on lipid and purine metabolism, decreases the incidence of cardiovascular events and has no negative effect on the uric acid level.
4. Meldonium digidratum - improves lipid profile and reduces the level of uric acid.
5. The combination of the BT, Losartan and Metamax is effective for lowering of atherogenic lipids and uric acid.
6. The strategy of managing patients with gout involves screening and correction of purine and lipid metabolism, to prevent the development of cardiovascular complications

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