

THE PHARMA INNOVATION - JOURNAL

Correction of Endothelial Dysfunction in Patients with Hypertension, Ischemic Heart Disease, Gout and Obesity

Maryana Vatsaba

1. Department of Internal Medicine № 2, SHEE “National Medical University (Ivano-Frankivsk)”, Ukraine.
[E-mail: vatsaba@yandex.ru; Tel: 0506983879]

Our study aimed to investigate the role of endothelial dysfunction in patients with hypertension, ischemic heart disease, gout and obesity. The study involved 41 patients (all male) with hypertension, ischemic heart disease, gout and obesity. The aim of research was to improve treatment of endothelial dysfunction in patients with hypertension, ischemic heart disease, gout and obesity by using Lozartan and Meldonium. Application to the basic therapy Lozartan and Meldonium improve the elastic properties of elastic arteries, particularly reduce endothelin-1, pulse wave velocity, aortic stiffness index, thickness intima - media complex and increase endothelium dependent vasodilatation. Thus, the combined use of Lozartan and Meldonium is feasible, effective and safe for prolonged use.

Keyword: Endothelial Dysfunction, Hypertension, Gout, Obesity.

1. Introduction

The main medical and social problem in Ukraine is growth of morbidity and prevalence of most prognostically unfavorable cardiovascular disease - hypertension and coronary heart disease^[5]. The decisive role in the growth of frequency of cardiovascular disease play such negative "wealth" as - sedentary lifestyle, chronic stress and increase calorie foods overweight and obesity^[2,6]. World Health Organization, is considered obesity to be the non-infectious epidemic of our time. By 2025 will be observed the increasing number of people with obesity. This diagnosis is almost in 50% of U.S. adults and 40% of the residents of Austria and England. Over a billion people on the planet have an overweight today^[7]. Prevalence of coronary heart disease, hypertension in patients with gout is significantly higher than in the general population^[8,3]. There are proven facts about early

and rapid development of atherosclerosis in patients with gout^[9].

Most patients with gout have more than two factors of cardio-vascular risk which are prognostically more unfavorable than having one cardiovascular factor^[3].

Therefore, the study of comorbidity of coronary artery disease with hypertension in patients with obesity and gout is a topical issue of general medical practice. Comorbidity and multimorbidity often are a cause of disability and reduced life expectancy^[4].

In the pathogenesis of comorbidity of coronary heart disease with hypertension endothelial dysfunction play an important role^[1].

The perspective is also such cardiovascular factor as a syndrome of early vascular aging. P. Nilson *et al*^[11] have formulated this concept, which was called Early Vascular Aging (EVA-syndrome), evolutionary roots of which can be slowing intrauterine development of the fetus, reduced

density of capillary network (capillary rarefaction), the development of endothelial dysfunction, reducing the diameter of the arteries and so on. The basis of EVA-syndrome is the reduction of the elastic properties of arteries and increasing of the arterial stiffness, the criteria of such condition is increasing of the velocity of the pulse wave, thickness intima-media complex, the level of endothelin-1 (ET-1), reduced endothelium-dependent vasodilation (EDVD). Increased arterial stiffness is associated with a lower content of elastin and increased collagen and some other qualitative changes in the arterial wall^[10,11].

2. Purpose:

To improve the treatment of patients with hypertension in combination with CHD, gout and obesity through the application of basic therapy in combination with the angiotensin receptor type 1 angiotensin II (losartan) and Meldonium (metamax).

3. Material and Methods

We examined 41 patients (all male) with hypertension of II degree with concomitant coronary heart disease, gout and obesity I-II grade, whose average age was 61.2 ± 1.8 years. The study included 15 healthy persons as control standards for performance. All patients were randomized into two groups: I group - 20 patients received basic therapy: prolonged nitrates, β -blockers, ACE inhibitors, aspirin and statin group II-21 patients except for BT additionally received losartan in a dose of 50-100 mg per day and meldonium (metamax) at a dose of 5 ml of 10% solution in 20 ml 0.9% sodium chloride intravenously for 10 days followed by transition to oral form (250 mg 2 times a day) for 1 month. Anthropometric study included determination of body mass index (BMI) measurement the circumference of the waist and hips, the ratio of waist circumference to hip circumference. It was found that all patients had an abdominal type of obesity (waist circumference / hip circumference $- (1.15-1.30)$ sm). Endothelial function was studied over the content of endothelin-1 in serum (ELISA). ASI

determined by the values of pulse pressure and stroke volume. TIMC set by dopplerography on the machine "Logiq 500" (Kranzbuhler, Germany) on an empty stomach, at room temperature 22 °C, with the patient lying on his back after 10-15 min rest. To determine endothelin dependent vasodilation (EDVD).

Statistical processing of the results was performed using Microsoft Excel 2010 and standard software package "Statistica 8.0 for Windows" ("Stat Soft", USA). Results are presented as mean (M) and average error (m). Chance of differences between dependent and independent options evaluated using Student t-test (the difference was considered significant at $p < 0.05$).

4. Results and Discussion

Evaluating the impact of basic therapy on the parameters of vascular aging syndrome received the following data (see Table 1). ASI decreased by 10.2% ($p < 0.05$), TIMC by 4.2% ($p < 0.05$), ET-1 on 12.74% ($p < 0.05$) and PWV by 9.5% ($p < 0.05$). EDVD increased by 41.0% ($p < 0.05$).

Using basic therapy in combination with losartan and Meldonium ASI reduced by 36.2% ($p < 0.001$). TIMC during the treatment according to the scheme of basic therapy with losartan and Meldonium decreased by 10.5% ($p < 0.001$). Analyzing the dynamics of ET-1, it was reduced by 46.88% ($p < 0.001$). EDVD increased by 86.6% ($p < 0.001$) with the use of basic therapy, losartan and Meldonium. PWV decreased by 31.6% ($p < 0.001$) using basic therapy, losartan and Meldonium.

5. Conclusions

Introduction to the basic therapy of hypertension in combination with ischemic heart disease, gout and obesity Meldonium and losartan can slow the progression of endothelial dysfunction and improve the elastic properties of elastic arteries, particularly reduce endothelin, cardio-ankle vascular index, pulse wave velocity, aortic stiffness index, thickness intima - media complex and increase endothelium dependent vasodilatation.

Table 1: Indicators of endothelial dysfunction in patients with hypertension, ischemic heart disease, gout and obesity during treatment (M±m)

Index	norm n=15	I group (n=21)		II group (n=20)	
		before treatment	after 1 month	before treatment	after 1 month
ASI, mm Hg/ml Δ%;p	0.61±0.02	0.98±0.01	0.88±0.03 -10.2 <0.05	0.99±0.01	0.63±0.04 -36.2 <0.001
TIMC, mm, Δ%;p	0.79±0.01	0.94±0.01	0.90±0.01 -4.2 <0.05	0.95±0.04	0.85±0.02 -10.5 <0.001
ET-1, ng/ml Δ%;p	6.23±0.14	17.42±0.89	15.2±1.31 -12.74 <0.05	18.75±0.89	9.96±0.56 -46.88 <0.001
EDVD, %, Δ%;p	13.89±0.8	5.5±0.79	7.76±0.75 +41.0 <0.05	6.9±0.79	12.88±0.8 +86.6 <0.001
PWV, m/s Δ%;p	9.4 ± 1.3	19.4±2.2	17.55±0.82 -9.5 <0.05	21.15±0.91	14.45 -31.6 <0.001

*Notices. ET-1 – Endothelin-1, EDVD – Endothelin dependent vasodilation, PWV – Pulse-wave velocity, ASI – Arterial stiffness index, TIMC – Thickness of the intima-media complex, p– value of the difference data in comparison with the values before treatment.

Obtained results suggest that signs of early vascular aging has better correction in response to the use of basic therapy in combination with losartan and Meldonium.

6. References

1. Buvaltsev V.I. Endothelial dysfunction as a new conception of prevention and treatment of cardiovascular diseases / V.I. Buvaltsev // International Journal of Medicine. - 2002. - № 2. - P. 202-205.
2. Denysyuk V.I. Endothelial dysfunction and insulin resistance in patients with hypertension "two sides of the same coin" / V. Denysyuk, H.I. Chrebtiy // CONSILIUM MEDICUM. - 2011. - Volume 5. Number 5. - P. 3-5.
3. Ilyin A.E. Gout, hyperuricemia and cardiovascular risk / A.E. Ilyin, V.G. Barskova, E.L. Nasonov // Scientific-Practical Rheumatology. - 2009. - № 1. - P. 56-63.
4. Kobalava J.D. Uric acid marker and / or a new risk factor for cardiovascular complications? / J.D. Kobalava, V.V. Tolkacheva, J.L. Karaulova // RMJ. - 2002. - 10. P. 431-436.
5. Mitchenko A.I. High cardiovascular risk in patients with hypertension and obesity / O. Mitchenko, V.Y. Romanov, K. Yanovska // Journal of Health of Ukraine. - 2012. - № 3-4. - P.24-25.
6. Mitchenko E.I. Obesity as a multidisciplinary problem: diagnosis, treatment, and prevention of complications / E.I. Mitchenko // Ukrainian Medical Journal. - 2012. - № 2 (89). - P. 19-21.
7. Obesity in the practice of cardiologist and endocrinologist / O. Bilovol, O.N. Kovalyov, S.S. Popov [et al.] // TSMU, Ukrainian medical book. - 2009. - P.616.
8. Puzanov O.G. Hyperuricemia and cardiovascular risk / O. Puzanov, A.I. Taran // Internal Medicine. - 2009. - № 3 (15). - P. 9-17.
9. Rudichenko V.M. Giperurikimeya, gout and the metabolic syndrome - a significant factor in the activity of a doctor family practice / V.M. Rudichenko // Science. visn. Nat. University-to O.O. Bogomoletc. - 2009. - № 2. - P. 180-187.
10. Nilson P.M. Introduction to Mini-symposium on developmental origins of adult disease / P.M. Nilson, A. Holmang // J. Internal. Med. - 2007. - Vol. 261. - P. 410-411.
11. Nilson P.M. The early life origins of vascular ageing and cardiovascular risk: the EVA syndrome (review) / P.M. Nilson, L. Lurbe, S. Laurent // J. Hypertension. - 2008. - Vol. 26. - P. 1049-1057.