Rapicka Dorota, Fabian-Danielewska Anna. Hyperuricemia and hypertension. Journal of Education, Health and Sport. 2019;9(7):233-239. eISSN 2391-8306. DOI http://dx.doi.org/10.5281/zenodo.3269865
http://ojs.ukw.edu.pl/index.php/johs/article/view/7124

The journal has had 7 points in Ministry of Science and Higher Education parametric evaluation. Part B item 1223 (26/01/2017).
1223 Journal of Education, Health and Sport eISSN 2391-8306 7

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 20.06.2019. Revised: 25.06.2019. Accepted: 05.07.2019.

Hyperuricemia and hypertension

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Summary

Hiperuricemia is associated mostly with gout and urolithiasis. However, it is now known that it affects a number of other health problems. It plays an important role in the development of hypertension, metabolic syndrome and other cardiovascular diseases. In addition, the relationship between hyperuricemia and obesity, hyperlipidemia, stroke and vascular dementia, renal disease, obstructive sleep apnea and insulin resistance has been proven. Increased serum uric acid is a risk factor for cardiovascular disease and contributes to increased mortality in patients with ischemic heart disease. The preferred drugs for the treatment of hypertension with increased uric acid concentration are calcium channel blockers (urinary properties) and losartan. From diuretics aldosterone antagonists are prefered. Other blockers of the angiotensin receptor should be

avoided because they reduce the excretion of uric acid by the kidneys. B-blockers, thiazide and loop diuretics, ACE inhibitors are also inadvisable.

Key words: *hyperuricemia; uric acid; gout; hypertension; metabolic syndrome; cardiovascular diseases;*

Admission

Hyperuricemia is associated mostly with gout and urolithiasis. However, it is now known that it affects a number of other health problems. It plays an important role in the development of hypertension, metabolic syndrome and other cardiovascular diseases. In addition, the relationship between hyperuricemia and obesity, hyperlipidemia, stroke and vascular dementia, renal disease, obstructive sleep apnea and insulin resistance has been proven.

Uric acid in humans is the final product of purine metabolism, which is distribute by enzymes. They form xanthines and hypoxanthines, which are then oxidized by xanthine oxidase to uric acid. The evolutionary lack of uricase is a factor increases the risk of hyperuricaemia. The concentration of uric acid in the blood should not exceed 6.8 mg / dl (404 umol/l), because above this value crystallization of monosodium urate occurs in an aqueous solution under physiological pH conditions and correct body warmth. Due to the inferior solubility of uric acid at a lower temperature, monosodalate urate crystals are the first to accumulate in less suppressed tissues, i.e. poorly vascularized or vascularized such as tendons, ligaments, and cartilage. Hyperuricemia may result from excessive endogenous synthesis, excessive supply of the diet, and uric acid renal excretion. They predispose certain clinical conditions, diseases and medications to elevated uric acid levels. [1,2,5,6]

Risk factors

Due to the possible long-term course of asymptomatic hyperuricaemia, it is worth to know the risk factors for its occurrence in everyday medical practice. The most important risk factors are:

- metabolic syndrome, overweight, hypertension
- eating habits - high consumption of meat, offal, seafood,
- medicines used (diuretics, low dose acetylsalicylic acid, cyclosporin),
- alcohol abuse,
- patients after organ transplants,
- male and postmenopausal women (estrogens promote kidney excretion of uric acid)
- advanced age
- genetic predisposition (primary hyperuricaemia)
- neoplasms
- diseases and clinical conditions resulting in reduction of renal excretion of uric acid (chronic kidney disease, ketoacidosis in the course of diabetes or reduced food intake)
- excessive physical exertion
- epilepsy
- endocrine diseases (hyperparathyroidism, hypothyroidism)

In patients with such risk factors, hyperuricemia should be suspected and appropriate diagnostics should be performed. [3,4,5]

Oxidant-Antioxidant paradox

Uric acid is an important antioxidant, stabilizing vitamin C and E, and directly inhibits free radicals by protecting the cell membrane and DNA. It inhibits intracellular mitochondrial oxidative stress, reduces the production of proinflammatory cytokines, interleukin IL-1, IL-6,

tumor necrosis factor alpha and activity of endothelial nitric oxide synthetase. Uric acid has the ability to prevent the acute activation of proinflammatory cells in the blood by oxidants, but at the same time it can not eliminate all oxygen radicals, such as superoxides. In addition, uric acid affects the proliferation of vascular smooth muscle cells resulting in dilated diarrhea and the formation of an inflammatory reaction within the vascular wall, oxidative stress, as well as an increase in the activity of renin. Hence, hyperuricemia is an independent risk factor for hypertension.

The European Society for Arterial Hypertension and the European Society of Cardiology recommend the study of serum uric acid in all patients with hypertension. Positive correlation between uric acid level and renal and peripheral vascular resistance has been demonstrated. In patients who suffer from hypertension with accompanying hyperuricemia, left ventricular hypertrophy and worse prognosis were more frequently demonstrated. [1,2,5,6,8]

Effect of hyperuricemia on the cardiovascular system

Increased serum uric acid is a risk factor for cardiovascular disease and contributes to increased mortality in patients with ischemic heart disease. Any increase in serum uric acid by 1mg/dl increases the risk of death from cardiovascular disease.

Hyperuricemia also shows association with type 2 diabetes, metabolic syndrome and insulin resistance. Abdominal obesity and high levels of BMI increase the production of insulin and leptin. Insulin stimulates the renin-angiotensin-aldosterone system, which increases uric acid resorption in the proximal urethra. In patients with type 2 diabetes, uric acid has been associated with systolic and diastolic blood pressure.

When hyperuricemia is diagnosed, one should begin to modify a lifestyle, quit smoking, and drink alcohol and use the right diet to reduce the risk of further increasing uric acid levels. Overweight and obese patient should also take care of the reduction of body weight and adequate

physical activity. The reduction in uric acid concentration is a prophylaxis of cardiovascular diseases in people with hyperuricaemia.

Increased concentration of uric acid also affects the development of atherosclerosis, contributes to the formation of thrombotic and ischemic changes. It is associated with an increased number of thrombocytes with altered structure and increased aggregation capacity. Hyperuricemia influences the endothelial cells by changing its functions and thus facilitating the formation of atherosclerotic plaque. [1,2,5,6,7]

Treatment of hypertension with hyperuricemia

The preferred drugs for the treatment of hypertension with increased uric acid concentration are calcium channel blockers (urinary properties) and losartan. From diuretics aldosterone antagonists are prefered. Other blockers of the angiotensin receptor should be avoided because they reduce the excretion of uric acid by the kidneys. B-blockers, thiazide and loop diuretics, ACE inhibitors are also inadvisable. [1,9]

Asymptomatic hyperuricemia- to treat, or not to treat ?

There is no straight answer to this question. The use of allopurinol at elevated uric acid levels without clinical symptoms is the prevention of vascular events. However, there is insufficient evidence, that such treatment would prevent gout, kidney disease or the occurrence of cardiovascular events. Treatment with allopurinol also has side effects, including vomiting, nausea, skin rash, hypersensitivity reactions, increased liver enzymes. It should be considered, whether the risk that such treatment brings with it, and the possible benefits of using xanthine oxidase inhibitors in the absence of symptoms of elevated uric acid in the body.

A non-pharmacological management of hyperuricemia should be preferred. Patients should increase physical activity, reduce weight, avoid alcohol consumption, drink sufficient amount of water, avoiding starvation and use a proper diet.

Current Polish recommendations suggests, that asymptomatic hyperuricaemia can be treated at uric acid levels above 12 mg% or when uric acid excretion in the urine exceeds 1100mg per day or when the cancer has disintegrated. [1,2,9]

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