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Original article

Asymptomatic Hyperuricemia as a Marker of Aggravation of Arterial Hypertension

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Abstract

Elevated serum uric acid (UA) concentration is considered to be as one of the factors contributing to endothelial dysfunction. However, it does not lead to clinical manifestations, so it is called asymptomatic hyperuricemia (ASH).

The purpose of research was to study the effect of ASH on arterial hypertension (AH) followed by its correction. The investigation was held from 2018 to 2019. The prevalence and degree of severity of ASH were studied in 1018 patients with AH. Hyperuricemia was discovered in 78 patients, which was 7.7% of the total number of studied patients.

Methods. A retrospective analysis of patients with AH undergoing inpatient treatment was performed. The control group of patients received standard hypotensive therapy. Although, the main group received standard therapy combined with urate-reducing therapy.

Results. Comparative analysis showed that hypotensive therapy was effective in both investigated groups. By the way, index of the main group experienced better results, i.e., the systolic blood pressure (SBP) decreased by 18 Hg (11.6%) compared to the control group. In terms of diastolic blood pressure (DBP), it is dropped by 11.8 Hg (12,1%). The positive effect of urate-reducing therapy is the reason for rising efficiency of the therapy at all. Moreover, significant decrease of UA level was experienced from both researched groups. It averaged 38,3 mmol/l, which is 39.2% of the original result.

Conclusion. Thus, the adverse effect of ASH on BP in patients with AH can be compensated by prescription of additional urate-reducing therapy to hypotensive drugs, which helps to reduce the adverse effect of ASH. The obtained data should be taken into account when physicians implement a disease management program.

Keywords: hypertension, risk factors, hyperuricemia, uric acid, biochemistry.

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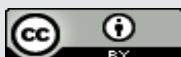
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Introduction

Arterial hypertension (AH) is a multifactorial disease which currently remains one of the most common diseases responsible for morbidity [1-3]. Recently, much attention has been paid to the problem of impaired functional state of the vascular endothelium leading to the progression of AH [4,5]. One of the factors contributing to endothelial dysfunction is elevated uric acid (UA) concentration, which does not lead to the clinical manifestations. It is called asymptomatic hyperuricemia (ASH) [6-8].

For many years, foreign and domestic literature sources note a pronounced relationship between increased UA and AH. ASH in patients with AH has more frequency than in the general population itself, from 25 to 50%. The incidence of ASH is even higher in patients with severe AH (up to 75%). The risk of AH soars by 40% with

Materials and methods

A retrospective analysis of patients with AH undergone inpatient treatment was performed. The investigation was held from 2018 to 2019. The prevalence and degree of severity of ASH were studied in 1018 patients with AH.

Hyperuricemia was discovered in 78 patients, which was 7.7% of the total number of studied patients. The level of UA over 360 $\mu\text{mol/L}$ in males and over 320 $\mu\text{mol/L}$ in females was considered as ASH [26], according to EULAR guidelines.

Subsequently, 60 patients aged from 45 to 75 years (mean age 58.3 ± 0.8 years) were selected by random sampling out of 78 patients.

Furthermore, 60 patients were separated to 2 groups - control ($n=30$) and main group ($n=30$) by random sampling. The control group received combined hypotensive therapy (ramipril + amlodipine), and in the

Results

The mean age of the patients was 61.8 ± 0.9 years among all respondents. The duration of AH was slightly more than 15 years. The mean value of adapted BP at the time of examination was nearly 146/87 mm/Hg. All patients were divided into age groups according to the age classification of the World Health Organization.

elevated UA levels [9-16]. Additionally, increased UA in patients with AH contributes to impaired renal function by increasing renal vascular resistance [17-18]. Hence, it is an important marker of renal damage and AH as a result [19-21].

European Society of Hypertension (ESH) (2018) and the European Society of Cardiology (ESC) declared that ASH is a brand-new factor of overall cardiovascular risk [22]. According to numerous literature data, UA carries on piquing an interest as a risk factor morbidity and mortality for cardiovascular patients [23-25].

The purpose of the study was to analyze the effect of ASH on the course of AH with its subsequent correction.

main group had the same therapy combined with urate-reducing drug allopurinol 200 mg daily. After 12 and 24 weeks of treatment, daily blood pressure monitoring (DBPM) and blood UA levels were performed and estimated.

The study did not include patients with symptomatic AH, diabetes mellitus, active inflammatory processes, coronary heart disease, chronic heart failure high functional class (III-IV by NYHA), gout, kidney, liver, blood diseases, and alcohol abuse.

Statistical processing of the obtained data was performed after creating a database in the Windows Excel system. Significance of the differences in the mean values was assessed by Student's t-test. The results were considered statistically significant if $p < 0.05$.

With regards the age composition of the respondents, it is apparent that elderly significantly prevailed over the other age categories and constituted 52% (Table 1). In terms of all age groups, as well as in the study as a whole, the number of women took over men (656 vs. 362).

Table 1 - Age-sex composition of patients with hypertension ($n=1018$)

Sex	Age	25-44 years old ($n=31$)	45-59 years old ($n=268$)	60-74 years old ($n=530$)	75-89 years old ($n=189$)
Male		5 (31.3%)	87 (32.4%)	208 (20.4%)	62 (6.1%)
Female		26 (68.7%)	181 (67.6%)	322 (60.7%)	127 (12.4%)
Total		31 (3.1%)	268 (26.3%)	530 (52.1%)	189 (18.5%)

The mean UA level in patients with ASH was significantly higher than in women, on average, by 66

$\mu\text{mol/L}$ (Figure 1). In addition, ASH in men was detected 30.6% more frequently than in women.

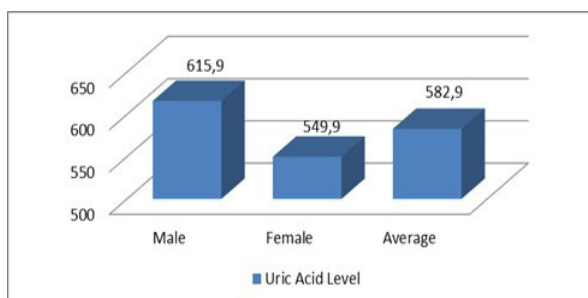


Figure 1 - Average uric acid levels by gender

We calculated the average UA level depending on the AH risk factor according to the SCORE scale to determine the link between the UA level of the patients and the AH risk group itself (Table 2). The results showed

that the UA ratio tended to increase depending on AH risk factors. Thus, the data suggest a significant increase in UA in patients with very high AH risk level.

Table 2 - Indicators of the UA level depending on the risk group of hypertension (n=78) (*p<0.02, **p<0.02, ***p<0.002)

AH risk factors	UA level (mmol/L)
Risk 1 (low)	489.3±2.53
Risk 2 (medium)	502.8±2.52*(p<0.02)
Risk 3 (high)	628.2±2.18**(p<0.02)
Risk 4 (very high)	711.5±1.92***(p<0.002)

According to the results of the data obtained after 12 weeks of treatment (Figure 2), both researched groups showed approximately similar figures in terms of the average SBP and DBP meanings. As for blood UA content, the index was significantly higher in the main

group. The decreasing in UA level by 5.4% (34.2 µmol/L) after 12 weeks of treatment appears to suggest that the inclusion of allopurinol contributes to the better results (p<0.05).

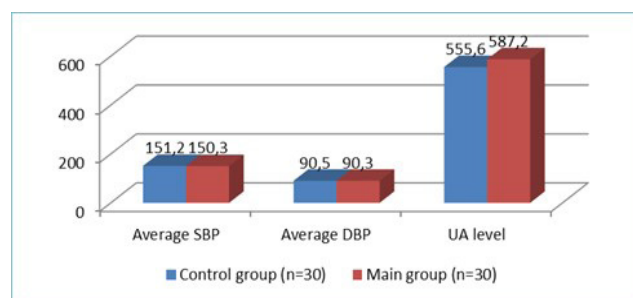


Figure 2 - The level of blood pressure and UA after 12 weeks of treatment. Note: the statistical significance of the differences (*p<0.05) is indicated in relation to patients of the control group

After 24 weeks of therapy, average SBP and DBP ratio in the main group decreased by 8.8 and 4.3 mmHg, correspondingly. As far as it concerns the same indexes of the control group, these dynamics were less significant (5.9 and 2.3 mmHg respectively).

µmol/l in the main group. The given information indicates a significant effect of allopurinol on the blood UA level after 24 weeks of therapy in AH patients in combination with ASH and indirectly on BP indices (Figure 3).

The UA level in the control group tended to increase. At the same time, this index fell down by 24.1

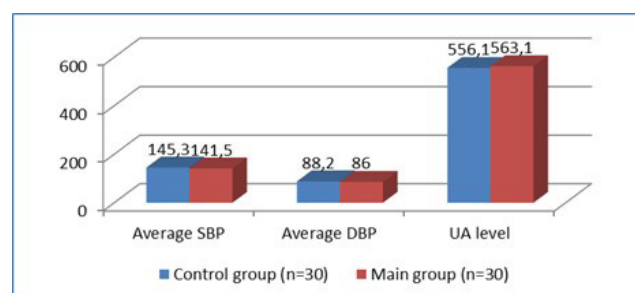


Figure 3 - The level of blood pressure and UA after 24 weeks of treatment. Note: the statistical significance of the differences (*p<0.05) is indicated in relation to patients of the control group

Discussion

Overall, a comparative analysis showed that antihypertensive therapy was effective in both groups. By the way, the average SBP decreased by 18±1.6 mm Hg in the main group compared to the control one, which was 11.6%, and the average DBP as well by 11.8±1.7 mm Hg (12.1%). What is more, the reason for more effective treatment is that the urate-lowering therapy had a positive effect, leading to a significant decrease in the level of UA in the blood serum by 38.3±1.4 mmol/l from the initial indicators, which was 39.2%.

The adverse effect of ASH on the blood pressure level in patients with hypertension can be compensated by the appointment of additional urate-lowering therapy to antihypertensive drugs, which helps to reduce such an effect of ASH on the course of hypertension.

The obtained data should be taken into account when the disease management program is implemented by general practitioners.

Limitations. Our work was not funded by governmental or non-governmental organizations. The translation of the article from the original language was

not made by a professional translator certified in the field of medicine.

Conclusions

How does this paper make a difference in general practice?

- The prescription of additional urate-reducing therapy helps to reduce the incidence of AH;
- The use of allopurinol contributes to a significant reduction in uric acid levels in patients with AH;
- Men are more prone to elevated blood levels of uric acid than women.

Conflicts of interest. Any potential and actual conflicts of interest were not met during our investigation.

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Authors' contributions. Conceptualization by Zh.N. and Zh.Zh.; writing (original drafting) by A.M., S.T., P.K.; writing (editing) by Zh.N., Zh.Zh.; data collection and processing - G.M.K., G.N.K. and E.L.

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Симптомсыз гиперурикемия артериалдық гипертензия агрессиясының маркері ретінде

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Түйіндіме

Эндотелий дисфункциясының дамуына ықпал ететін факторлардың бірі қан сарысуындағы зәр қышқылының жоғары концентрациясы болып табылады, ол клиникалық көріністердің дамуына әкелмейді және асимптоматикалық гиперурикемия деп аталады.

Зерттеудің мақсаты асимптоматикалық гиперурикемияның артериялық гипертензия ағымына әсерін зерттеу, оны кейіннен түзету болып табылады.

Әдістері. Стационарлық емделуде болған артериялық гипертензиясы бар науқастарға ретроспективті талдау жүргізілді. Зерттеу 2018 жылдан 2019 жылға дейін жүргізілді. Артериалды гипертензияның таралуы мен оның ауырлық дәрежесі жалпы саны 1018 науқаста зерттелді. Гиперурикемия 78 науқаста анықталды, бұл зерттелген науқастардың жалпы санының 7,7% құрады.

Нәтижелері. Салыстырмалы талдау екі топтағы гипотензивті терапияның тиімді екенін көрсетті. Бірақ негізгі топта бұл көрсеткіштер жақсырақ болды. Сондықтан систолалық артериялық қан қысымы орташа көрсеткіші $18 \pm 1,6$ мм рт.ст. төмендеді. Бақылау тобында бұл көрсеткіш орташа есеппен $11,8 \pm 1,7$ мм рт.ст. (12,1%) құрады. Неғұрлым тиімді емдеудің себебі ураттың мөлшерін төмендетуші ем оң әсер етті деп есептейміз. Яғни қан сарысуындағы зәр қышқылы деңгейінің бастапқы көрсеткіштерден $38,3 \pm 1,4$ мкмоль/л-ге сенімді төмендеуіне алып келіп, 39,2%-ні құрады.

Қорытынды. Осылайша, асимптоматикалық гиперурикемия бар науқастарда қан қысымы деңгейіне аурудың қолайсыз әсері гипотензивті препараттарға қосымша ураттың мөлшерін төмендетуші ем тағайындаумен өтелуі мүмкін. Бұл артериялық гипертензия ағымына асимптоматикалық гиперурикемияның қолайсыз әсерін төмендетуге ықпал етеді. Алынған деректерді алғашқы медициналық-санитарлық көмек дәрігерлерінің ауруды басқару бағдарламасын іске асыру кезінде ескеру қажет.

Түйін сөздер: артериялық гипертензия, қауіп-қатер факторлары, гиперурикемия, зәр қышқылы, биохимия.

Бессимптомная гиперурикемия как маркер обострения артериальной гипертензии

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Резюме

Одним из факторов, способствующих развитию эндотелиальной дисфункции, является повышенная концентрация мочевой кислоты (МК) в сыворотке крови, которая не приводит к развитию клинических проявлений и называется бессимптомной гиперурикемией (БГУ).

Целью исследования явилось изучение влияния бессимптомной гиперурикемии на течение артериальной гипертензии с последующей ее коррекцией.

Методы. Проводился ретроспективный анализ пациентов с артериальной гипертензией, находившихся на стационарном лечении. Исследование проводилось с 2018 по 2019 гг. Изучена распространенность и степень тяжести БГУ у 1018 пациентов с артериальной гипертензией. Гиперурикемия выявлена у 78 больных, что составило 7,7% от общего числа обследованных больных.

Результаты. Сравнительный анализ показал, что гипотензивная терапия в обеих группах была эффективной, но в основной группе эти показатели были лучше, так средний показатель САД снизился на $18 \pm 1,6$ мм рт.ст. по сравнению с контрольной группой, что составило 11,6%, а средний показатель ДАД на $11,8 \pm 1,7$ мм рт.ст. (12,1%). Причиной более эффективного лечения считаем, что уратснижающая терапия оказала положительное влияние, приводя к достоверному снижению уровня МК в сыворотке крови на $38,3 \pm 1,4$ мкмоль/л от первоначальных показателей, что составило 39,2%.

Выводы. Таким образом, неблагоприятное влияние БГУ на уровень АД у пациентов с артериальной гипертензией, может быть компенсировано назначением дополнительной уратснижающей терапии к гипотензивным препаратам, что способствует снижению неблагоприятного влияния БГУ на течение артериальной гипертензии. Полученные данные необходимо учитывать при реализации программы управления заболеванием врачами первичной медико-санитарной помощи.

Ключевые слова: артериальная гипертензия, факторы риска, гиперурикемия, мочевая кислота, биохимия.