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Assessment of cholecalciferol and antihypertensive therapy concomitant use in people with arterial hypertension

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Abstract. Background. The purpose of the study was to assess the effect of cholecalciferol intake at a daily dose of 2,000 IU on the serum level of 25(OH)D total and blood pressure (BP) against the background of antihypertensive therapy in people with arterial hypertension (AH) stage II. **Materials and methods.** We performed a prospective, single-center study of 115 individuals with AH stage II (91 females and 24 males), mean age 50.7 ± 7.1 years. The duration of the follow-up period averaged 15.8 ± 1.8 months (from 12 to 18 months). The patients were receiving antihypertensive therapy according to the European guidelines: angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists — losartan, or diuretics (hydrochlorothiazide or indapamide) as a part of combination therapy, or calcium antagonists — amlodipine, or beta-adrenergic blockers, or their combination. Every second patient was recommended to take vitamin D in the form of cholecalciferol at a dose of 2,000 IU/d daily. All subjects were performed full blood count, clinical urine examination, measure of fasting blood sugar, serum urea, serum creatinine, office systolic and diastolic blood pressure, anthropometric data, electrocardiography. Serum level of total vitamin D was determined using immunoassay. Statistical analysis was done by using software package STATISTICA 10.0 (SN AXAR207F394425FA-Q). **Results.** It was found that intake of diuretics (hydrochlorothiazide at a dose of 12.5–25.0 mg or indapamide 1.5 mg) as a part of combination antihypertensive therapy influenced the dynamics of serum 25(OH)D ($F = 5.35$; $p = 0.02$) and its level ($F = 11.8$; $p = 0.0009$). Dynamics of SBP value was highest (-27.4 ± 17.9) in the group receiving a diuretic and cholecalciferol, which was significantly ($p < 0.001$) different from the comparison group. In the same group, we established a correlation relationship between SBP dynamics and length of cholecalciferol intake ($R = 0.42$; $p = 0.023$). A significant influence of both cholecalciferol ($F = 4.1$; $p = 0.046$), and diuretics ($F = 14.3$; $p = 0.0003$) on SBP dynamics was established. **Conclusions.** Thiazide/thiazide-like diuretics negatively influenced the improvement of serum 25(OH)D level. The combined use of cholecalciferol and diuretic at a dose of 2,000 IU/day in the treatment of patients with AH II degree allowed to obtain the greatest hypotensive effect on SBP without the risk of vitamin D overdosing in the body. **Keywords:** arterial hypertension; cholecalciferol; antihypertensive therapy; diuretics

Introduction

Reduction in vitamin D level in the body is viewed as a potential risk factor for arterial hypertension (AH) [1, 2], low level of 25(OH)D is associated with increased level of blood pressure (BP) [2–6] and increased incidence of AH [7]. According to the European guidelines [1], individuals with cardiovascular diseases, AH in particular, belong to the risk group for whom it is recommended to determine the level of 25(OH)D since untreated vitamin D deficiency can significantly reduce efficiency of the background therapy or change the disease course. At present, the findings of more than 50 studies including supplementary intake of various vitamin D preparations (D_2 (ergocalciferol), D_3 (cholecalciferol), calcitriol (1,25-hydroxyvitamin D_3) etc.) with assessment of their effect on the values of systolic (SBP) and diastolic blood pressure (DBP) [8] are available. Duration of vitamin D intake in these studies varied from 2 weeks to 12 months. In all studies the doses of vitamin D higher than 600 IU a day (from 800 to 8,571 IU per day) were used. The

highest effect on lowering SBP was described in a placebo-controlled study [9] in patients with diabetes mellitus type 2. According to that study, single intake of ergocalciferol at a dose of 100,000 IU demonstrated a 14 mm Hg reduction in SBP as compared to the placebo group.

Considering the fact that AH is a wide-spread disease and has an independent continuous relationship with the incidence of a number of cardiovascular events (stroke, myocardial infarction, sudden death, cardiac failure, end-stage renal disease), achieving the BP target level is one of the main tasks of the administered antihypertensive therapy [10, 11]. In view of modern data it is essential both to optimize the level of 25(OH)D in the body of people with AH and to choose maximum effective vitamin D dosages and regimens of intake when included into the combination therapy of AH.

Purpose of the study was to assess the effect of cholecalciferol intake at a daily dose of 2,000 IU on the serum level of 25(OH)D total and BP against the background of antihypertensive therapy in people with AH stage II.

Materials and methods

We conducted a prospective single-center study of 115 individuals with AH stage II (91 females and 24 males), their mean age being 50.7 ± 7.1 years. The duration of follow-up period averaged 15.8 ± 1.8 months, from a minimum of 12 months to a maximum of 18 months. Verification of AH diagnosis, stage and risk was performed according to the European guidelines (2013) [11]. Research protocol was approved by the Committee for Biomedical Ethics of Grodno State Medical University. All subjects underwent full blood count, clinical urine examination, fasting blood sugar, serum urea, serum creatinine tests. Results in all cases were normal. Venous blood samples were taken after the overnight fast, 12–14 hours after the last intake of food and medications. All patients had electrocardiography, office systolic and diastolic blood pressure measurement, and their anthropometric data were taken. During the overall follow-up period all patients were receiving antihypertensive therapy according to the European guidelines: either angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor antagonists (ARA) — losartan, or diuretics (hydrochlorothiazide or indapamide) as a part of combination therapy, or calcium antagonists (CA) — amlodipine, beta-adrenergic blockers (β -blockers) or their combination.

Vitamin D status was assessed according to the serum level of vitamin D total ($25(\text{OH})\text{D}$ total = $25(\text{OH})\text{D}_3 + 25(\text{OH})\text{D}_2$) using immunoenzymatic assay with original DRG reagents (Germany, Marburg) at the premises of the Scientific Research Laboratory of Grodno State Medical University. We used singularly de-frozen plasma for analysis. According to the European guidelines [11], vitamin D level was considered optimal with $25(\text{OH})\text{D}$ total 30–80 ng/ml, insufficient with $25(\text{OH})\text{D}$ total 20–30 ng/ml, deficient with $25(\text{OH})\text{D}$ total < 20 ng/ml.

$25(\text{OH})\text{D}$ total was assessed at baseline, at 3 months and at the end of the follow-up period. Every second patient on the alphabetical list, in addition to antihypertensive therapy, was recommended to take vitamin D in the form of cholecalciferol at a dose of 2,000 IU/d daily. After three months, the patients were invited by telephone to the polyclinic to have a 25-hydroxyvitamin D blood test taken, BP was also measured, and antihypertensive therapy was corrected when necessary. Seventy-two patients were receiving cholecalciferol for three months, 20 of these continued the intake of cholecalciferol for 6 months, 9 persons continued the intake for an average of 8.7 ± 2.1 months.

Statistical analysis was performed using Statistica 10.0 (SN AXAR207F394425FA-Q). Data representation corresponded to the character of their distribution: in normal distribution (by Shapiro-Wilk test) — as a mean and standard deviation ($M \pm SD$), in non-normal distribution — as a median (Me) and interquartile range [Q25–Q75]. To assess the association between the variables we used Spearman rank correlation analysis (R). To estimate the influence of several factors on the value of the studied index, we used ANOVA multivariate analysis of variance (Kruskal-Wallis test, Median test). Two dependent groups of the studied variables were compared according to the Wilcoxon test. When the number of groups was more than

two, and for pair-wise comparison of significant differences between the groups, the Duncan's test was used. The index “dynamics” (d) was calculated as a difference between values before and after administered therapy. The nil hypothesis was rejected at $p \leq 0.05$.

Results

During the follow-up period, 38.8 % of subjects were receiving monotherapy with antihypertensive drugs, 50.9 % were receiving combined therapy with two preparations, 6.6 % were receiving three preparations. According to the group of antihypertensive drugs, the patients were divided into the following groups: 87.7 % subjects were receiving ACE inhibitors/ARA, 37.7 % were receiving thiazide or thiazide-like diuretics, 16 % were on CA, 18.9 % were on β -blockers.

At baseline, office SBP and DBP averaged 150 [140; 160]/90 [90; 100] mm Hg, heart rate — 73.3 ± 10.4 beats/min, height 166.6 ± 8.6 cm, weight 85.9 ± 17.5 kg, body mass index (BMI) 30.9 ± 5.8 kg/m². Over 15.8 ± 1.8 months of follow-up there was a significant ($p < 0.0001$) reduction in both office SBP and DBP, their means averaged 130 [125; 140] and 80 [80; 90] mm Hg correspondingly, while the HR did not change ($p = 0.37$) and was 71.7 ± 13.3 beats/min. Target levels of BP as for the results of office measurements were achieved in 83.9 % and 87.1 % of cases for SBP and DBP levels correspondingly.

Serum $25(\text{OH})\text{D}$ total in the whole group of the studied patients at baseline was 24.8 [17.02; 34.06] ng/ml, at the end of the follow-up period — 41.7 [33.1; 53.5] ng/ml ($p = 0.00001$).

We also analyzed the effect of certain groups of antihypertensive drugs on the dynamics of serum $25(\text{OH})\text{D}$ total and its level at the end of the follow-up. It was established that administration of diuretics (hydrochlorothiazide at a dose of 12.5 mg and higher, or indapamide at a dose of 1.5 mg and higher) influenced the dynamics of serum $25(\text{OH})\text{D}$ ($F = 5.35$; $p = 0.02$) and its level ($F = 11.8$; $p = 0.0009$).

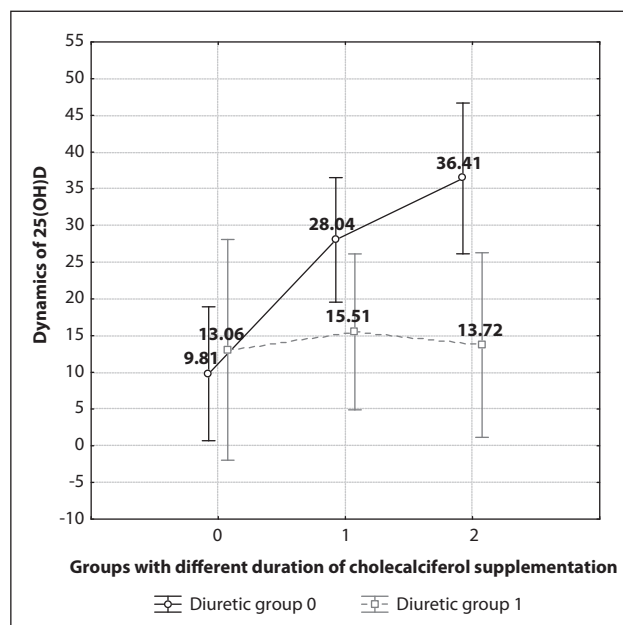


Figure 1. Dynamics of $25(\text{OH})\text{D}$ level in groups without intake (0) and with intake (1) of diuretics

As shown in Figure 1, the highest 25(OH)D dynamics was in the group of those patients who were not receiving diuretics at the background of long-term (6 months and longer) ingestion of cholecalciferol (36.4 [25.1; 47.7], $p < 0.05$) as compared to the values of the dynamics in all groups apart from one group consisting of individuals who received cholecalciferol for 3 months but did not receive diuretics either. In the group of patients, who received thiazide/thiazide-like diuretics, serum 25(OH)D dynamics after a year of the follow-up made up 13.7 [8.9; 19.9], which was lower ($p < 0.05$) than in the group without intake of diuretics. Serum 25(OH)D dynamics as well as its level at the end of the follow-up were not significantly influenced by the intake of other groups of antihypertensive drugs (ACE inhibitors, ARA, β -blockers, CA).

Taking into consideration the data described above, all the studied patients with AH stage II were divided into the following groups:

— group 0 — those receiving neither a diuretic as a part of combination antihypertensive therapy, nor cholecalciferol for correction of vitamin D level in the body;

— group 1 — those not receiving a diuretic but taking cholecalciferol at 2,000 IU/d;

— group 2 — those not receiving cholecalciferol, but taking a diuretic as a part of combination antihypertensive therapy;

— group 3 — those taking both a diuretic and cholecalciferol at 2,000 IU/d.

Medians and interquartile range of the studied indices and their dynamics are shown in Table 1. Comparison of the above groups according to the intake of other preparation groups (ACEi/ARA, CA, β -blockers) as a part of combination antihypertensive therapy did not reveal any significant differences (Kruskal-Wallis test). The groups were also matched ($p > 0.05$) for age, BMI, DBP level. SBP level was significantly higher in group 3 as compared to group 0 and group 1 (see Table 1).

At baseline, the groups did not differ in terms of serum 25(OH)D total level ($p > 0.05$ in all cases). Following the therapy, optimal serum 25(OH)D total level was observed in 82.3 % of subjects of group 0, in 92 % of group 1, in 72.7 % of group 2, and in 79.3 % of group 3, while the duration of cholecalciferol intake was comparable ($p > 0.05$) and amounted to 4.5 ± 2.3 months in group 1, 4.4 ± 2.2 months in group 3. The highest average level of serum 25(OH)D total after the therapy was observed in group 1 (see Table 1) and the comparison of the above groups (Kruskal-Wallis test) showed significant differences between group 1 and group 0 ($p = 0.04$), group 2 ($p = 0.02$), group 3 ($p = 0.002$). In group 1 the dynamics of 25(OH)D total was maximal — 32.3 [18.8; 49.6] and significantly higher than in group 0 ($p = 0.0009$), group 2 ($p = 0.05$) and group 3 ($p = 0.02$).

At the end of the follow-up, the groups did not differ according to SBP, DBP levels and DBP dynamics ($p > 0.05$ in all cases); however there were differences in SBP dynamics. As indicated in Table 1 and Figure 2, SBP dynamics was maximal (-27.4 ± 17.9) in group 3 and, as revealed by the analysis of variance (Duncan's test), it was significantly different from all groups: from group 2 (-17.3 ± 14.9 ; $p = 0.04$); from group 1 (-9.6 ± 14.7 ; $p = 0.0007$) and from group 0 (-8.7 ± 16.1 ; $p = 0.0005$). Similar findings were obtained when using other methods of statistical analysis for comparing dSBP between the groups by means of Median test ($\chi^2 = 8.99$; $p = 0.0295$) and by Kruskal-Wallis test ($H = 19.08397$; $p = 0.0003$).

In all subjects with AH stage II, we established a significant correlation between intake of a diuretic and SBP dynamics ($R = -0.41$; $p = 0.000017$). We established a significant influence of cholecalciferol administration on SBP dynamics ($F = 4.1$; $p = 0.046$), as well as a significant influence of diuretic intake on SBP dynamics ($F = 14.3$; $p = 0.0003$). Besides, in group 3 there was established

Table 1. Indices of blood pressure and 25-hydroxyvitamin D in groups of patients according to the administered treatment

Indices		Group 0	Group 1	Group 2	Group 3
n		29	37	11	29
SBP, mm Hg	baseline	141.6 \pm 11.0	142.7 \pm 13.1	151.8 \pm 13.3	156.5 \pm 13.7 ^{#,1}
	after therapy	132.9 \pm 14.9	133.1 \pm 13.7	134.6 \pm 15.1	129.1 \pm 12.3
	dynamics	-8.7 \pm 16.1	-9.6 \pm 14.7	-17.3 \pm 14.9	-27.4 \pm 17.9 ^{#,1,2}
DBP, mm Hg	baseline	90.1 \pm 8.3	91.2 \pm 8.1	94.6 \pm 8.2	92.8 \pm 6.9
	after therapy	83.4 \pm 7.9	84.2 \pm 8.9	85.9 \pm 8.0	80.7 \pm 9.2
	dynamics	-6.40 \pm 12.99	-7.0 \pm 10.4	-8.6 \pm 9.5	-12.1 \pm 11.2
25(OH)D, ng/ml, baseline		32.9 (27.7; 41.2)	22.6 (16.5; 33.4)	27.9 (13.3; 33.8)	23.5 (14.7; 29.2)
25(OH)D, ng/ml, after 3 months of cholecalciferol intake		—	36.3 (31.0; 65.5)	—	32 (29.2; 42.2)
d 25(OH)D over 3 months		—	17.7 (8.1; 46.4)	—	13.6 (-2.4; 24.8)
25(OH)D, ng/ml, after therapy		41.4 (31.9; 49.7)	53.5 (41.3; 68.4) ^{#,2,3}	39.6 (29.2; 42.7)	37.4 (30.4; 47.6)
d 25(OH)D		10.7 (-4.7; 21.0)	32.3 (18.8; 49.6) ^{#,2,3}	11.5 (0.7; 22.9)	15.6 (7.2; 21.5)

Note: significant differences ($p < 0.05$): [#] — significant differences as compared to group 0; ¹ — significant differences as compared to group 1; ² — significant differences as compared to group 2; ³ — significant differences as compared to group 3 (Kruskal-Wallis test).

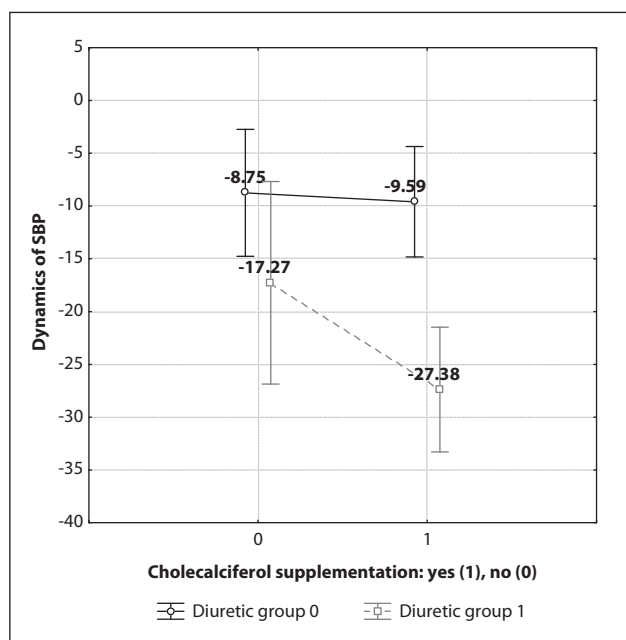


Figure 2. Dynamics of SBP in groups without cholecalciferol and diuretic (group 0), with intake of cholecalciferol (group 1), with intake of diuretic (group 2), with diuretic + cholecalciferol (group 3)

a correlation between SBP dynamics and duration of cholecalciferol intake ($R = 0.42$; $p = 0.023$).

Having distributed the examined subjects with AH into subgroups according to the intake of ACEi/ARA, CA, β -blockers with or without cholecalciferol intake, we did not obtain similar convincing and significant findings concerning the influence on either SBP or DBP during concomitant use of a diuretic and cholecalciferol.

Discussion

Over the recent 5 years, there have been published several meta-analyses of randomized, placebo-controlled studies evidencing BP reduction with supplementary intake of vitamin D [8, 12, 14]. One of the first meta-analyses demonstrated a significant reduction in SBP (-6.2 mm Hg, 95% CI from -12.32 to -0.04) and DBP (-3.1 mm Hg, 95% CI from -5.5 to -0.6) in subjects with AH but not in normotensive patients as compared to placebo [12]. The meta-analysis performed in 2014 [13] showed a significant reduction only in DBP (-1.31 , 95% CI -2.28 , -0.34 mm Hg, $P = 0.01$) for subjects with cardiovascular diseases. Data of the recent meta-analysis which included 46 studies (4,541 participants) did not demonstrate a significant reduction either in SBP or DBP in supplementary intake of vitamin D [8].

Simultaneously, there has been a continuous debate about what level of serum 25-hydroxyvitamin D should be considered optimal, what doses and dosage frequency of vitamin D preparations are necessary to obtain the optimum. Although $25(\text{OH})\text{D} > 30$ ng/ml is postulated to be optimal for health in general, there are no results indicating what level is necessary for obtaining maximal antihypertensive effect. The doses and forms of vitamin D preparations also vary greatly in the studies. In the recent

meta-analysis [8], most studies used either small doses of vitamin D preparations or intermittent dosage regimens (daily, monthly or less often). Intermittent dosage regimens can have different biological effects as compared to small regular doses. Moreover, results of meta-analysis make it difficult to differentiate the role of low serum 25-hydroxyvitamin D level from other important cardiovascular risk factors (age, obesity, smoking etc.) which also influence not only baseline level of vitamin D in the body but its dynamics as well.

Analysis of literature data revealed single studies which evaluated the results of concomitant use of antihypertensive drugs and vitamin D but we did not find any publications where diuretics were referred to as an antihypertensive group. In our study, the patients were not on monotherapy with diuretics either, the latter were used as a part of combination therapy with ACEi or ARA. More often, results of the studies referred to the fact of using antihypertensive drugs in a certain percentage of cases or in connection with group of patients who received ACEi. However, absence of significant associations between $25(\text{OH})\text{D}$ level and BP in subjects receiving ACEi does not rule out the possibility of such associations. Due to the effect of ACEi on renin-angiotensin-aldosterone system, it is impossible to establish additional hypotensive effect of vitamin D, whose influence on BP is, first and foremost, explained by its ability to suppress renin and angiotensin II secretion [14–17]. Moreover, it has been established that suppression of renin secretion by vitamin D through activation of its receptors occurs irrespective of calcium and parathyroid hormone homeostasis and changes of water-electrolyte exchange [15].

Of interest are the results of double blind placebo-controlled study of people with AH stage I–II in which CA nifedipine at a dose of 30 mg/d was used as a part of antihypertensive therapy and the participants were divided into two groups with supplementary intake of vitamin D ($n = 63$, 2,000 IU/d) or placebo ($n = 63$). Ambulatory monitoring of BP was performed three times — at baseline, after 3 and 6 months of the follow-up. In the group of patients who received vitamin D there was a significant increase in serum $25(\text{OH})\text{D}$ level (from 19.4 ± 11.6 ng/ml to 34.1 ± 12.2 ng/ml at 6 months, $p < 0.001$). Furthermore, in this group as compared to the placebo, after 6 months there was a significant ($p < 0.001$) reduction observed in SBP by 6.2 mm Hg and in DBP by 4.2 mm Hg. The researchers came to the conclusion that administration of vitamin D preparations resulted in BP reduction and could be used as adjuvant therapy for patients with AH stage I–II [18].

We are also aware of interesting results from a prospective randomized placebo-controlled study [19] of 283 healthy individuals who were divided into four groups: those taking placebo, cholecalciferol at a dose of 1,000, 2,000 and 4,000 IU/d respectively. BP was measured in all subjects at baseline, after 3 and 6 months. There were no changes in DBP values, while SBP values ($p = 0.04$) changed significantly during the follow-up. At 3 months in group 1, increase in SBP by 1.7 mm Hg was observed, while in group 2, SBP decreased by 0.66 mm Hg, and in groups 3 and 4 — by 3.4 and 4.0 mm Hg respectively. The authors

made the following conclusion from the data received: the higher the dose of cholecalciferol, the lower SBP values. Moreover, BP values had a significant reverse correlation with serum 25(OH)D level.

Thus, current literature data concerning efficiency of vitamin D supplementary intake by people with AH or by healthy individuals are ambivalent and even contradictory.

Conclusions

1. Supplementary intake of cholecalciferol at a dose of 2,000 IU/d in people with AH stage II at the background of antihypertensive therapy for 4.4 ± 2.2 months without a diuretic allows to optimize vitamin D level in 92 % of cases while with a diuretic — in 79 % of cases. Thiazide/thiazide-like diuretics negatively influence the increase of serum 25(OH)D total level. The intake of other groups of antihypertensive drugs — ACEi, ARA, CA, β -blockers — does not influence significantly the dynamics of 25(OH)D total.

2. Duration of cholecalciferol intake is directly correlated with SBP dynamics.

3. Concomitant use of a diuretic (hydrochlorothiazide at a dose of 12.5 mg or indapamide 1.5 mg) and cholecalciferol at a dose of 2,000 IU/d in therapy of AH stage II allows to obtain the highest hypotensive effect on SBP values without the risk of vitamin D overdosing, and thus should be used in clinical practice.

Conflicts of interests. Authors declare the absence of any conflicts of interests that might be construed to influence the results or interpretation of their manuscript.

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Оцінка поєднаного застосування холекальциферолу і антигіпертензивної терапії в осіб з артеріальною гіпертензією

Резюме. Актуальність. Метою дослідження стала оцінка впливу застосування холекальциферолу в дозі 2000 МО на добу на рівень 25(ОН)D у сироватці й артеріальний тиск на фоні антигіпертензивної терапії у хворих з артеріальною гіпертензією II стадії. **Матеріали та методи.** Ми провели проспективне одноцентрове дослідження в 115 хворих із II стадією АГ (91 жінка та 24 чоловіки), середній вік $50,7 \pm 7,1$ року. Тривалість періоду спостереження становила в середньому $15,8 \pm 1,8$ міс. (від 12 до 18 міс.). Пацієнти отримували антигіпертензивну терапію відповідно до європейських рекомендацій: інгібітори ангіотензинперетворюючого ферменту або антагоністи рецепторів ангіотензину — лозартан, або діуретики (гідрохлортиазид або індапамід) у складі комбінованої терапії, або антагоністи кальцію — амлодипін, або бета-адреноблокатори, або їх поєднання. Кожному другому пацієнтові було рекомендовано приймати вітамін D у вигляді холекальциферолу в дозі 2000 МО/день щоденно. Усім пацієнтам проводили загальний аналіз крові, загальний аналіз сечі, визначення цукру в крові натще, сечовини в сироватці крові, креатиніну в сироватці крові, систолічного і діастолічного артеріального тиску, антропометричних даних, електрокардіографію. Рівень загального вітаміну D в сироватці крові визначали за допомогою імуноферментного аналізу. Статистичний аналіз про-

дили, використовуючи програмний пакет «STATISTICA 10.0» (SN AXAR207F394425FA-Q). **Результати.** Було виявлено, що прийом діуретиків (гідрохлортиазиду в дозі 12,5–25 мг або індапаміду в дозі 1,5 мг) у складі комбінованої антигіпертензивної терапії впливає на зміни 25(ОН)D у сироватці ($F = 5,35$; $p = 0,02$) і його рівень ($F = 11,8$; $p = 0,0009$). Зміни систолічного артеріального тиску були більш виражені ($-27,4 \pm 17,9$) у групі пацієнтів, які отримували діуретик і холекальциферол, відносно групи порівняння, що відповідало рівню вірогідності $p < 0,001$. У тій же групі був виявлений взаємозв'язок між динамікою систолічного артеріального тиску й тривалістю прийому холекальциферолу ($R = 0,42$; $p = 0,023$). Було виявлено вірогідний вплив як холекальциферолу ($F = 4,1$; $p = 0,046$), так і діуретиків ($F = 14,3$; $p = 0,0003$). **Висновки.** Тіазидні або споріднені діуретики мають негативний вплив на рівень 25(ОН)D у сироватці. Одночасне застосування холекальциферолу й діуретика в дозі 2000 МО на добу для лікування пацієнтів з АГ II стадії дозволяє досягти найбільшого антигіпертензивного ефекту щодо систолічного артеріального тиску без ризику надлишкової концентрації вітаміну D в організмі.

Ключові слова: артеріальна гіпертензія; холекальциферол; антигіпертензивна терапія; діуретики

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Оценка сочетанного применения холекальциферола и антигипертензивной терапии у лиц с артериальной гипертензией

Резюме. Актуальность. Целью исследования стала оценка влияния применения холекальциферола в дозе 2000 МЕ в сутки на уровень 25(ОН)D в сыворотке и артериальное давление на фоне антигипертензивной терапии у больных с артериальной гипертензией II стадии. **Материалы и методы.** Мы провели проспективное одноцентровое исследование у 115 больных со II стадией АГ (91 женщина и 24 мужчины), средний возраст $50,7 \pm 7,1$ года. Продолжительность периода наблюдения составила в среднем $15,8 \pm 1,8$ мес. (от 12 до 18 мес.). Пациенты получали антигипертензивную терапию в соответствии с европейскими рекомендациями: ингибиторы ангиотензинпревращающего фермента или антагонисты рецепторов ангиотензина — лозартан, или диуретики (гидрохлортиазид или индапамид) в составе комбинированной терапии, или антагонисты кальция — амлодипин, или бета-адреноблокаторы, или их сочетание. Каждому второму пациенту было рекомендовано принимать витамин D в виде холекальциферола в дозе 2000 МЕ/день ежедневно. Всем пациентам проводили общий анализ крови, общий анализ мочи, определение сахара в крови натощак, мочевины в сыворотке крови, креатинина в сыворотке крови, систолического и диастолического артериального давления, антропометрических данных, электрокардиографию. Уровень общего витамина D в сыворотке крови определяли с помощью иммуноферментного анализа. Статисти-

ческий анализ выполняли, используя программный пакет «STATISTICA 10.0» (SN AXAR207F394425FA-Q). **Результаты.** Было выявлено, что прием диуретиков (гидрохлортиазид в дозе 12,5–25 мг или индапамида в дозе 1,5 мг) в составе комбинированной антигипертензивной терапии оказывает влияние на изменения 25(ОН)D в сыворотке ($F = 5,35$; $p = 0,02$) и его уровень ($F = 11,8$; $p = 0,0009$). Изменения систолического артериального давления были более выражены ($-27,4 \pm 17,9$) в группе пациентов, получавших диуретик и холекальциферол, в отличие от группы сравнения, что соответствовало уровню достоверности $p < 0,001$. В той же группе была выявлена взаимосвязь между динамикой систолического артериального давления и длительностью приема холекальциферола ($R = 0,42$; $p = 0,023$). Было обнаружено достоверное влияние как холекальциферола ($F = 4,1$; $p = 0,046$), так и диуретиков ($F = 14,3$; $p = 0,0003$). **Выводы.** Тиазидные или тиазидоподобные диуретики оказывают отрицательное влияние на уровень 25(ОН)D в сыворотке. Сочетанное применение холекальциферола и диуретика в дозе 2000 МЕ в сутки для лечения пациентов с АГ II стадии позволяет достичь наибольшего антигипертензивного эффекта в отношении систолического артериального давления без риска избыточной концентрации витамина D в организме.

Ключевые слова: артериальная гипертензия; холекальциферол; антигипертензивная терапия; диуретики