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INFLUENCE OF ETHYLMETHYLHYDROXYPYRIDINE SUCCINATE INCLUSION IN ANTIHYPERTENSIVE THERAPY ON THE CONDITION OF THE ARTERIAL WALL IN YOUNG PATIENTS WITH HYPERTENSION

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The purpose of the study was to evaluate the impact of combined antihypertensive therapy including ethylmethylhydroxypyridine succinate on blood pressure levels, arterial stiffness and quality of life in young patients with hypertension. A total of 60 patients (mean age, 41.7±1.3 years) with grade 2 hypertension who were not taking regular antihypertensive therapy were examined. After baseline data collection, 30 patients (group 1) were administered basic therapy with antihypertensive drugs and ethylmethylhydroxypyridine succinate, and 30 patients (group 2) were administered basic therapy, which included a combination of lisinopril 10–20 mg/day and amlodipine 5–10 mg/day for 8 weeks. After the treatment, a decrease in systolic and diastolic blood pressure levels in groups 1 and 2 by 23.3 mm Hg and 17.5 mm Hg and 14.3 mm Hg and 8.4 mm Hg, respectively, was observed (all p<0.05). It was found that average daily levels of systolic and diastolic blood pressure were 7.1 % and 10.8 % (p<0.05) lower in the patients of group 1 compared to group 2 and had a positive effect on daily BP profiles. A more significant decrease in the pulse wave velocity in the aorta was observed (2.1±0.5 m/s, p<0.05) in group 1, while in group 2 this parameter decreased by (1.5±0.5 m/s, p<0.05). There was an improvement in the scale scores representing physical health, working capacity, psychological abilities, degree of severity of negative psychological state, as well as the ability to social contacts more expressed in group 1. Therefore, inclusion of ethylmethylhydroxypyridine succinate in the therapeutic complex in young patients with hypertension increases efficacy of antihypertensive therapy, improves daily blood pressure profiles and positively affects the quality of life in this category of patients.

Key words: hypertension, young age, combined antihypertensive therapy, ethylmethylhydroxypyridine succinate, arterial stiffness, quality of life.

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ВПЛИВ ДОДАВАННЯ ЕТИЛМЕТИЛГІДРОКСИПІРИДИНУ СУКЦИНАТУ ДО АНТИГІПЕРТЕНЗИВНОЇ ТЕРАПІЇ НА СТАН АРТЕРІАЛЬНОЇ СТІНКИ У ПАЦІЄНТІВ МОЛОДОГО ВІКУ З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ

Метою дослідження було оцінити вплив комбінованої антигіпертензивної терапії з додаванням етилметилгідроксипіридину сукцинату на рівні артеріального тиску, показники артеріальної ригідності та якості життя у пацієнтів молодого віку з артеріальною гіпертензією. Обстежено 60 пацієнтів (середній вік 41,7±1,3 роки) з артеріальною гіпертензією 2 ступеня, які не приймали регулярну антигіпертензивну терапію. Після реєстрації вихідних даних 30 пацієнтам (1 група) призначали базисну терапію АГ та етилметилгідроксипіридину сукцинату та 30 пацієнтам (2 група) призначали базисну терапію, що включала комбінацію лізиноприлу 10–20 мг/добу і амлодипіну 5–10 мг на добу протягом 8 тижнів. Після проведеного лікування встановлено зменшення рівнів систолічного та діастолічного артеріального тиску в 1 і 2 групах на 23,3 мм рт.ст. і 17,5 мм рт.ст. та 14,3 мм рт.ст. і 8,4 мм рт.ст. відповідно (усі p<0,05). Показано, що середньодобові рівні систолічного та діастолічного артеріального тиску були на 7,1 % і 10,8 % (p<0,05) нижчі у пацієнтів 1 групи в порівнянні з 2 групою та позитивний вплив на добові профілі АТ. Встановлено більше зниження ШППХ на (2,1±0,5 м/с, p<0,05) в 1 групі, тоді як у 2 групи ШППХ вменшувалась на (1,5±0,5 м/с, p<0,05). Спостерігалось поліпшення показників шкал, що відображають фізичне самопочуття, працездатність, психологічні здібності, ступінь вираженості негативного психологічного самопочуття, а також здатність до соціальних контактів більш виражене в 1 групі пацієнтів. Таким чином, включення в терапевтичний комплекс етилметилгідроксипіридину сукцинату у пацієнтів з артеріальною гіпертензією молодого віку підвищує ефективність гіпотензивної терапії, поліпшує добові профілі АТ та позитивно впливає на якість життя у цієї категорії хворих.

Ключові слова: артеріальна гіпертензія, молодий вік, комбінована антигіпертензивна терапія, етилметилгідроксипіридину сукцинат, артеріальна ригідність, якість життя.

The work is a fragment of the research project "To determine the features of immunocytokine imbalance in comorbid patients with arterial hypertension and type 2 diabetes and cardiovascular and renal complications", state registration No. 0123U101711.

Recent decades have been characterized by an increase in the prevalence of arterial hypertension (AH) among the adult population. According to the World Health Organization, increased blood pressure (BP) is the leading risk factor for mortality in the world [11]. The current tendency is an increasing AH among young people, which is a serious problem all over the world [6]. It has been established that high

BP has a strong, independent and linear relationship with the risk of cardiovascular disease, cerebral stroke, myocardial infarction and renal failure [2, 14]. However, it should be noted that insufficient effectiveness of antihypertensive therapy remains a significant problem [7, 8].

Oxidative stress and chronic inflammation have been identified as potentially responsible for the development of endothelial damage and vascular stiffness, two of the primary mechanisms of AH and cardiovascular disease [6].

The mechanism of cytoprotectors is associated not only with the hemodynamic effect, but also with a positive effect on the mechanisms of energy production and consumption, with their ability to optimize the function of the respiratory system, to correct the balance between antioxidant protection and activity of free radical oxidation mechanisms. The advantage of ethylmethylhydroxypyridine succinate is in combination with the antihypoxant and antioxidant action of its components, namely succinic acid with oxypyridine. Evaluation of the effectiveness of medications that could be actively involved in intracellular metabolic processes, combat the negative effects of oxidative stress syndromes, chronic systemic inflammation in young patients with AH seems promising and reasonable.

The purpose of the study was to evaluate the impact of combined antihypertensive therapy with ethylmethylhydroxypyridine succinate on blood pressure levels, arterial stiffness and quality of life in young patients with hypertension.

Materials and methods. The study included 60 patients between the ages of 35 and 44 years (mean age 41.7 ± 1.3 years), including 40 men and 20 women, with grade 2 AH who did not receive regular antihypertensive therapy.

After registration of baseline data, 30 patients (group 1) were prescribed a complex therapy that included basic AH therapy and ethylmethylhydroxypyridine succinate (100 mg orally three times a day) for 8 weeks. The comparison group (group 2) consisted of 30 patients who were prescribed basic therapy, which included a combination of lisinopril 10–20 mg/day and amlodipine 5–10 mg per day. Patients in both groups also received statins and antiplatelet therapy. These groups of patients were comparable in terms of age and sex. The control group consisted of 20 healthy individuals (mean age 40.9 ± 1.2 years).

The study was performed in accordance with the standards of proper clinical practice and the principles of the Declaration of Helsinki.

Exclusion criteria for the study: secondary forms of AH, professional athletes, grade 3 AH, IHD, history of stroke, chronic renal failure, cardiac arrhythmias, severe comorbidities (external respiratory system, endocrine system, oncological diseases, etc.)

The standard method of examination of a patient included clinical and laboratory-instrumental studies in accordance with the recommendations of the European Society of AH / European Society of Cardiology (ESH/ESC, 2018).

Daily blood pressure monitoring (DMBP) was performed using the ABPM-02 device (Meditech, Hungary). The following were evaluated: mean values of systolic (SBP) and diastolic blood pressure (DBP), mean BP daily (24 hours), day and night, time index (TI) of hypertension – % of measurements of $SBP \geq 140$ and $DBP \geq 90$ mm Hg during the period of activity; and, respectively, ≥ 120 and ≥ 70 mm Hg during sleep. The severity of the biphasic day-night BP rhythm was assessed by the daily index (DI), which was calculated by the formula:

$$DI = 100 \% \times (BPd - BPn) / BPd,$$

where BPd is the average BP during activity; BPn is the average BP during sleep.

Four groups of patients were classified according to the value of DI:

- “dipper” (DI – 10 – 20 %) – optimal nocturnal BP lowering;
- “non-dipper” (DI – 0 – 10 %) – insufficient nocturnal BP reduction;
- “night-picker” (DI < 0) – persistent increase in nocturnal BP;
- “over-dipper” (DI > 20) – excessive nocturnal BP reduction.

Parameters of central aortic pressure and arterial stiffness were examined by the method of applanation tonometry using the SphygmoCor-PVx device (AtCor Medical Pty Ltd, Australia) according to the standard methods recommended by the experts in the assessment of arterial stiffness (Laurent S., 2006). The program automatically calculated the levels of SBP, DBP in the aorta and main characteristics of the central pulse wave (aortic incremental pressure (AP), systolic peak amplitudes P1, P2, incremental index – augmentation index.

(AIx=AP/PT P2/P1), including normalized one to 75 beats/min HR (AIx@HR 75). Pulse wave velocity in the aorta (PWV) was measured with the same device by sequentially recording of the pulse wave on the carotid and femoral arteries and simultaneously recording of the ECG signal in three chest leads. To calibrate the carotid artery waves, the system was entered with the mean and diastolic aortic

blood pressure values obtained from the radial artery measurements. The value of the PWV was calculated by the formula:

$$PWV = D / \Delta t,$$

where D is the distance between the jugular notch and the level of the umbilicus (m); Δt is the difference between the time from the Q wave to the beginning of the signal in the ascending and abdominal aorta (s).

The Marburg University General Well-Being Questionnaire (GWBQ, J. Siegrist et al., 1989) was used to assess patients' quality of life. The questionnaire includes 7 clinical scales: patients' assessment of their physical condition (I), work capacity (II), positive (III) or negative (IV) psychological condition, psychological abilities (Y), interpersonal relationships (YI) and social abilities (YII scale). During the assessment of the dynamics of the GWBQ scales, it was taken into account that a decrease in the scores on the I and IV scales and an increase in the other scales indicates an improvement in the quality of life.

The mathematical computer processing of the study results was performed using the Statistica 10.0 software package (Statsoft Inc, USA) with standard algorithms of variational statistics. During analysis of intergroup differences in indices, the Student's T-test was calculated. In the case of indices measured on a nominal scale, the reliability of differences in the frequency of detection of an indicator in two compared groups was assessed by Student's t-test using Fisher's transformation, and linear correlation coefficients and rank correlations were calculated. Differences in mean values and correlations were considered reliable at a significance level of $p < 0.05$.

Results of the study and their discussion. The dynamics of BP indices according to sphygmomanometry and DMBP are presented in Table 1.

Table 1.

Changes in office BP and DMBP in the process of treatment of young AH patients (M \pm m)

Indices	Group 1 (n=30)		Group 2 (n=30)	
	Before treatment	After treatment	Before treatment	After treatment
Sphygmomanometry: SBP, mm Hg	149.7 \pm 5.1	126.4 \pm 3.2**	148.8 \pm 5.0	131.3 \pm 3.3**
DBP, mm Hg	91.6 \pm 5.3	77.3 \pm 2.5*	92.5 \pm 4.2	84.1 \pm 2.3*
DMBP:				
SBP24, mm Hg	144.8 \pm 3.2	120.1 \pm 2.6*	142.3 \pm 3.1	128.6 \pm 3.1*
DBP 24, mm Hg	89.4 \pm 3.1	73.1 \pm 2.0***	89.9 \pm 3.3	81.0 \pm 2.1*
TI SBP day, %	41.2 \pm 9.7	17.3 \pm 5.3*	46.3 \pm 9.3	17.7 \pm 5.4*
TI DBP day, %	28.6 \pm 4.4	15.1 \pm 2.8*	29.1 \pm 4.5	15.7 \pm 2.8*
TI SBP night, %	32.6 \pm 7.1	14.1 \pm 5.1*	33.8 \pm 6.5	14.4 \pm 5.3*
TI DBP night, %	20.4 \pm 4.8	12.1 \pm 3.4	25.7 \pm 5.3	14.1 \pm 4.6

Notes: 1. * – reliability of differences in comparison with the baseline data; 2. * – $p < 0.05$; 3. ** – $p < 0.01$; 4. *** – $p < 0.001$.

In our study, after 8 weeks of continuous antihypertensive therapy with administration of ethylmethylhydroxypyridine succinate, a decrease in office BP was observed: SBP – by 23.3 mm Hg and DBP – by 14.3 mm Hg and in the comparison group by 17.5 and 8.4 mm Hg, respectively. At the same time, 100 % of patients in group 1 and 93.3 % of patients in group 2 reached the target BP level.

The analysis of DMBP after the course of treatment revealed high antihypertensive efficacy of both treatment regimens (Table 1), but it was more pronounced in the case of ethylmethylhydroxypyridine succinate administration ($p < 0.05$). Thus, average daily SBP and DBP were 7.1 % and 10.8 % ($p < 0.05$) lower in patients of group 1 compared with group 2.

Indices of pressure load in all patients after the treatment including ethylmethylhydroxypyridine succinate decreased. TI of hypertension in terms of SBP and DBP significantly decreased in all time intervals, but did not exceed the norm, indicating a stable 24-hour antihypertensive effect.

The analysis of the changes in the types of diurnal BP curves according to DMBP showed that in group 1 the number of “dippers” increased significantly from 9 (30 %) to 30 (100 %) ($p < 0.05$) due to the transfer of 21 (70 %) non-dippers to the “dipper” group. Less pronounced changes were found in patients of group 2: the number of “dippers” increased from 8 (26.7 %) to 21 (70 %) ($p < 0.05$), the number of “non-dippers” decreased from 22 (73.3 %) to 9 (30 %) ($p < 0.05$).

Changes in central aortic pressure in young patients with AH are shown in Fig. 1.

By comparing the contribution of medications to the degree of reduction of central SBP, it was found that after 8 weeks of treatment, the highest reduction occurred in group 1 in comparison with group 2 ($\Delta 18.7 \pm 1.9$ mm Hg and $\Delta 14.7 \pm 1.5$ mm Hg) ($p < 0.05$).

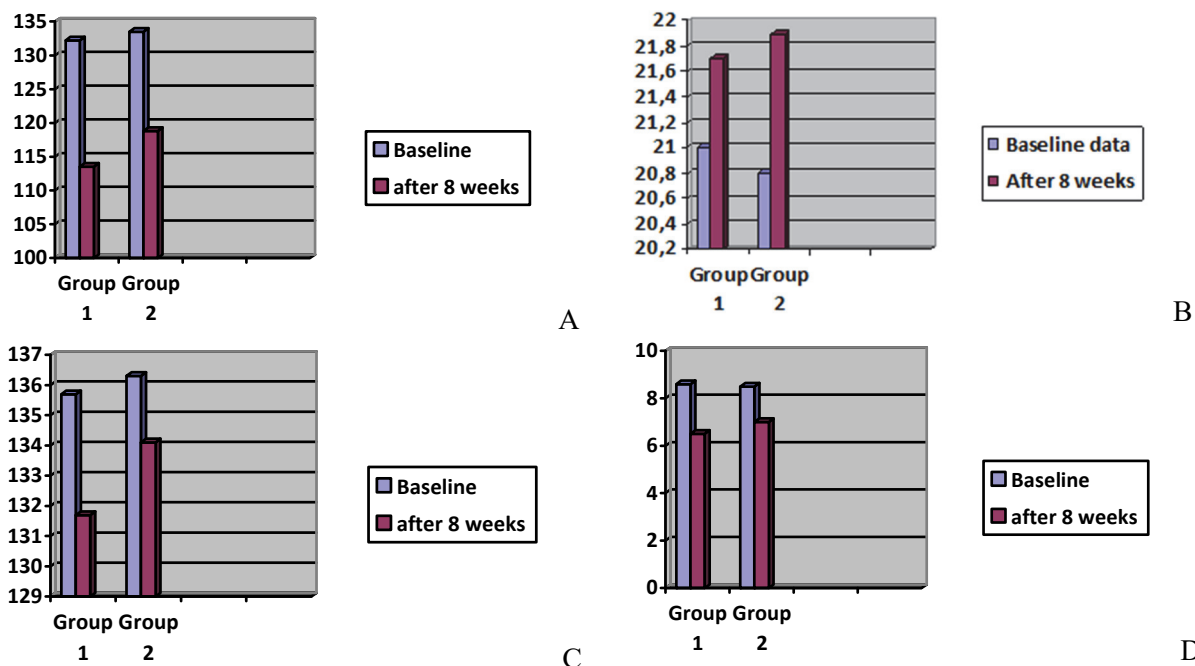


Fig. 1 Dynamics of SBP in the aorta (mm Hg) (A), Aix@HR75 (%) (B), pulse pressure amplification (%) (C) and pulse wave velocity (D) in young patients with hypertension due to the influence of therapy.

In our study, during the observation period, medication therapy led to a decrease in the parameters of vascular stiffness after 8 weeks of treatment. After the treatment, we observed a decrease in PWV by (2.1±0.5 m/s, p<0.05) in patients of group 1 and by (1.5±0.5 m/s, p<0.05) in the comparison group.

Complex therapy supplemented with ethylmethylhydroxypyridine succinate positively influenced the indices characterizing the quality of life of young patients with AH (Table 2).

Table 2

Changes in the indices of quality of life (M±m, in points) during the treatment of young patients with AH

GWBQ scales	The period of study	Group 1 (n=30)	Group 2 (n=30)
I	Before treatment	7.62±0.41	7.63±0.42
	After treatment	6.03±0.40*	6.06±0.41*
II	Before treatment	13.51±0.40	13.53±0.41
	After treatment	15.08±0.35**	14.71±0.32**
III	Before treatment	8.27±0.40	8.28±0.42
	After treatment	8.81±0.35	8.83±0.36
IY	Before treatment	11.09±0.36	11.01±0.37
	After treatment	8.51±0.33**	9.85±0.33*
Y	Before treatment	14.45±0.33	14.43±0.35
	After treatment	16.49±0.31**	15.36±0.32*
YI	Before treatment	7.54±0.43	7.53±0.44
	After treatment	7.35±0.40	7.41±0.42
YII	Before treatment	12.71±0.53	12.70±0.53
	After treatment	13.99±0.41*	13.34±0.43*
C	Before treatment	3.75±0.10	3.77±0.11
	After treatment	3.99±0.12	3.94±0.12
H	Before treatment	4.18±0.17	4.16±0.20
	After treatment	4.44±0.18	4.40±0.21

Notes: Abbreviations: S – state of health a week before the study; M – mood a week before the study. 1. * – reliability of differences compared to the baseline data; 2. * – p<0.05; 3. ** – p<0.001.

After the treatment, there was a significant improvement in the indices of the questionnaire's I, II, IY, Y and YII scales, covering almost all the components of quality of life in both groups of patients. At the same time, in group 1, a greater (p<0.05) improvement in the psychological component of quality of life was found: psychological abilities (Y scale) and the degree of severity of negative psychological health of the examined patients (IY scale). Improvement of physical well-being (I scale) of patients of both groups was determined (probably as a result of BP correction). There was also a tendency for a more positive impact of combination therapy with the introduction of ethylmethylhydroxypyridine succinate on the ability to work (II scale), ability to make social contacts (YII scale) in young patients with AH.

Over the past few decades, AH in young individuals has become a serious public health problem all over the world [13]. The most significant risk factors for the development of AH are: family history of early cardiovascular diseases in the family, smoking, excessive body weight, hypercholesterolemia, and hypodynamia [13]. The today tendency is a steady increase in the number of psychotraumatic, frustrating and stressogenic factors that negatively affect a person, his or her professional life and health [5]. The system of cardiovascular regulation is the most responsive to the influence of negative social and psychological factors that play an important role in the onset and development of AH in most patients.

Despite the current potential of pharmacological agents and nonpharmacological methods of AH treatment, the level of reaching target blood pressure values in patients with AH remains insufficient [7]. Results of clinical trials have shown that central aortic pressure is a better prognostic factor for cardiovascular events compared to peripheral pressure [12].

Ethylmethylhydroxypyridine succinate belongs to the group of antioxidants and, according to some experimental studies, it improves the functioning of the ischemic myocardium and contractile function of the heart, reduces manifestations of left ventricular dysfunction [9]. At the same time, this drug exhibits anxiolytic, stress-protective and nootropic effects. The action of ethylmethylhydroxypyridine succinate is based on its antioxidant, antihypoxic and membrane-stabilizing activity and its ability to reduce damaging effect of free radicals on cells [3].

In our study, additional administration of ethylmethylhydroxypyridine succinate along with standard combination antihypertensive therapy contributed to a more pronounced reduction in BP, which is consistent with the previous studies [1, 4]. Clinical studies [10] have shown that combined antihypertensive therapy had a positive effect on the elastic properties of the aorta and its branches. According to our data, additional administration of ethylmethylhydroxypyridine succinate allowed to reduce the levels of central systolic aortic pressure and PWV more effectively, what indicates an improvement in the elastic properties of blood vessels.

Consequently, the inclusion of ethylmethylhydroxypyridine succinate in the therapeutic complex in young patients with AH increases efficacy of antihypertensive therapy, improves daily blood pressure profiles, and positively affects the quality of life in this category of patients.

Conclusions

1. Combined antihypertensive therapy with administration of ethylmethylhydroxypyridine succinate in young patients with AH leads to a more pronounced reduction in SBP and DBP levels based on sphygmomanometry and daily BP monitoring, along with the correction of pathological types of daily BP profile in comparison with the antihypertensive therapy group.
2. The inclusion of ethylmethylhydroxypyridine succinate in the complex therapy of AH in young patients is more beneficial for the reduction of central blood pressure and pulse wave propagation velocity.
3. Complex therapy supplemented with ethylmethylhydroxypyridine succinate positively affected the quality of life of young patients with AH. An improvement was observed in the scores of scales reflecting physical health, performance, psychological abilities, degree of severity of negative psychological state, and ability to socialize.

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STATISTICAL STUDY OF THE INFLUENCE OF FOOD PRODUCTS ON THE OCCURRENCE OF CARIES AND PERIODONTITIS IN PERSONS AGED 18–22 YEARS

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The article presents the results of the study on the food products influence on caries and periodontal processes using statistical methods. The information base of the study was the data obtained by surveying dental students aged 18–22 years of the medical university. Mainly, consumption of dairy products, vegetables and fruits, meat, bread, and sweets were considered as factors. The quantitative characteristic of nutrition was taken as the number of food consumption times during the week. The hypothesis that the amount of food consumption affects the state of the periodontium and the number of carious teeth in a person has been confirmed. As a result of determining the relevant dependencies, a significant influence of two food products groups – dairy and vegetables and fruits – was revealed. Directly, the dependences have a non-linear (quadratic) form, and accordingly, the optimal intervals of the products consumption are established, since both insufficient and excessive use of them negatively affects the condition of the teeth and gums. A two-factor linear statistical dependence was built to estimate the total effect of two types of food products. Regarding other products, no significant relationships were found between their use and the oral cavity condition. The conclusions of the article present the main results of the performed studies and directions for further research.

Key words: caries, periodontal disease, food products, statistical dependence, impact assessment, optimal consumption

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СТАТИСТИЧНЕ ДОСЛІДЖЕННЯ ВПЛИВУ ПРОДУКТІВ ХАРЧУВАННЯ НА ВИНИКНЕННЯ КАРІЕСУ ТА ПАРОДОНТИТУ У ОСІБ ВІКОМ 18–22 РОКІВ

В статті подані результати дослідження впливу харчових продуктів на процеси карієсу та пародонту з застосуванням статистичних методів. Інформаційною базою дослідження послужили дані, які отримані шляхом анкетування студентів-стоматологів віком 18–22 роки медичного університету. В основному як фактори розглядалось вживання молочних продуктів, овочів і фруктів, м'яса, хліба, солодощів. За кількісну характеристику харчування приймалась кількість разів споживання продуктів протягом тижня. Підтверджено гіпотезу, що кількість споживання продуктів впливає на стан пародонту та кількість карієсних зубів у особи. В результаті визначення відповідних залежностей виявлено суттєвий вплив двох груп харчових продуктів – молочних та овочів і фруктів. Безпосередньо залежності мають нелінійний (квадратичний) вигляд і відповідно встановлено оптимальні інтервали обсягів споживання продуктів, оскільки як недостатнє, так і надлишкове їх вживання негативно впливає на стан зубів і ясен. Побудована двофакторна лінійна статистична залежність, яка дає можливість оцінити сумарну дію двох видів продуктів харчування. Стосовно інших продуктів, то суттєвих взаємозв'язків між їх вживанням та станом ротової порожнини не виявлено.

Ключові слова: карієс, пародонт, продукти харчування, статистична залежність, оцінка впливу, оптимальне споживання.

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Rational nutrition is an integral part of a healthy human lifestyle [1, 2] and plays a significant role in the prevention of major dental diseases (tooth caries, gingivitis, periodontitis, etc.) [10, 11]. This influence of rational nutrition is expressed in the aspect of the teeth formation, resistant to the influence of adverse factors, such as, for example, the cariogenic effect of simple carbohydrates, the insufficient amount of necessary trace elements and vitamins, etc.[4–6].