Реферати

ЗАСТОСУВАННЯ НАНОКРИСТАЛІВ ДЛЯ ЛІКУВАННЯ ХРОНІЧНОГО ВЕРХІВКОВОГО ПЕРІОДОНТИТУ

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Застосування нанокристалів для лікування хронічного верхівкового періодонтиту – сучасний рівень наномедицини. Нами обстежено та пролiковано 11 хворих віком від 17 до 67 років на загострений та хронічний верхівковий періодонтит за допомогою авторської методики з використанням фосфатного буферу. Проведена оцінка клінічних та рентгенологічних даних підтвердила процес відновлення періапікальних тканин у 11 пацієнтів. Вона показала, що регенерація верхівкових та прилеглих до них ділянок періодонту в 10 випадках мали позитивну динаміку вже через 29-30 днів від початку лікування; у 1 випадку – відмічена сповільнена динаміка відновлення через 40 днів від початку лікування через наявність у пацієнта соматичної патології. Запропонований спосіб лікування хронічного верхівкового періодонтиту на підставі отриманих результатів лікування потребує подальшого вивчення у віддалені терміни з метою широкого впровадження в практичну стоматологію.

Ключові слова: лікування хронічного верхівкового періодонтиту, монокристали, фосфатний буфер.

Стаття надійшла 30.06.2019 р.

ПРИМЕНЕНИЕ НАНОКРИСТАЛЛОВ ДЛЯ ЛЕЧЕНИЯ ХРОНИЧЕСКОГО ВЕРХУШЕЧНОГО ПЕРИОДОНТИТА

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Применение нанокристаллов для лечения хронического верхушечного периодонтита - современный уровень наномедицины. Нами обследовано и пролечено 11 больных в возрасте от 17 до 67 лет на обострившийся и хронический верхушечный периодонтит с помощью авторской методики использования фосфатного буфера. Проведена оценка клинических и рентгенологических данных, которые подтвердили процесс восстановления периапикальных тканей у 11 пациентов. Она показала, что регенерация верхушечных и прилегающих к ним участков периодонта в 10 случаях имели положительную динамику уже через 29-30 дней от начала лечения; в 1 случае - отмечена замедленная динамика восстановления через 40 дней от начала лечения из-за наличия у пациента соматической патологии. Предложенный способ лечения хронического верхушечного периодонтита на основании полученных результатов лечения требует дальнейшего изучения в отдаленные сроки с целью широкого внедрения в практическую стоматологию.

Ключевые слова: лечение хронического верхушечного периодонтита, монокристаллы, фосфатный буфер.

Рецензент Аветіков Д.С.

DOI 10.26724/2079-8334-2020-3-73-65-69
UDC 616.151.1:616.12 – 008.331.1:616 – 056.52:616.379 – 008.61

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DIETARY CORRECTION OF HYPERINSULINEMIA AND HEMOSTASIS PARAMETERS IN OVERWEIGHT ARTERIAL HYPERTENSION PATIENTS

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The purpose of our study was to investigate the influence of a carbohydrate-restricted diet up to 250 g per day for 12 weeks on body mass index, insulin level, and parameters of hemostasis in patients with arterial hypertension and metabolic disorders. It was registered the decrease in the body mass index by 7%, insulin level by 27.8%, factor von Willebrand activity (p=0.009) and soluble fibrin content (p=0.03) and the improvement of the platelet aggregation induced by ADP and ristocetin in patients with arterial hypertension and increased body mass index who followed the diet with carbohydrate restriction up to 250 g per day for 12 weeks in addition to standard therapy. A diet with carbohydrate restriction up to 250 g per day should be recommended to the patients with combination of arterial hypertension, increased body mass index and hyperinsulinemia in addition to antihypertensive therapy.

Key words: arterial hypertension, carbohydrate-restricted diet, body mass index, insulin level, hemostasis parameters.

The study is a fragment of the research project "Hemodynamic and coronary blood supply disturbances and ectopical myocardial activity in patients with ischemic heart disease and diabetes mellitus, methods of correction", state registration No. 0117U006000.

The scientific debate concerning optimal management of patients with arterial hypertension (AH) is still open despite effective recommendations for lifestyle modification and medicines [1]. This is connected predominantly with high incidence of complications associated with AH, notably stroke and cardiovascular diseases [2]. Furthermore, risk of complications increases drastically in patients with metabolic disorders [3]. For instance, it was reported a 2-fold increase in cardiovascular outcomes and 1.5-fold increase in all-cause mortality [2].

Variety methods for correction of metabolic dysfunction and associated disorders exist [4]. The effectiveness of carbohydrate-restricted diets was showed in numerous studies [5]. However, the data of carbohydrate-restricted diets impact on hemostasis is still insufficient, although the crucial role of the latter in pathogenesis of AH complications and metabolic disorders is undoubted [6].

In our study we investigated parameters of vascular hemostasis and coagulation in patients with basic treatment and additional carbohydrate-restricted diet.

The purpose of our study was to investigate the influence of a carbohydrate-restricted diet up to 250 g per day for 12 weeks on body mass index (BMI), insulin level, and parameters of vascular hemostasis and coagulation in patients with combination of AH, increased BMI and hyperinsulinemia, and to assess impact of this diet on course of disease.

Material and methods. The present study included 50 patients aged between 27 and 64 years old with AH, increased BMI and hyperinsulinemia (29 females and 21 males). This population was divided into two groups. 26 patients of group I (control group) received standard antihypertensive therapy, they were recommended to follow healthy life style and dietary habits. 24 patients of group II (main group) received a diet with carbohydrate restriction up to 250 g per day for 12 weeks in addition to standard therapy and healthy life style. The content of carbohydrates in diet was controlled by carbohydrate counting tables. Daily caloric intake was compensated with higher fats and proteins consumption. Standard therapy depending on peculiarities of patients included angiotensin converting enzyme inhibitor (ACEi) or angiotensin II receptors blocker (ARB), sometimes with diuretic or ACEi with calcium channels blocker (CCB) or ARB with CCB, beta-adrenergic blocker, statin and antiaggregant.

The effectiveness of therapy was controlled by measurement of day-time office BP.

AH was diagnosed according to the current guidelines [1]. 11 patients suffered from stable angina (SA) functional class (FC) I-II. 4 patients had DM II. The patients included into the research had been under observation for the period of 12 weeks.

BMI was calculated with metric formula as measured weight in kilograms divided by height in meters squared. WHO criteria were used to define nutritional status of patients.

BP measurements were obtained following a standard protocol.

We used vWF:CBA ELISA Kit to measure the binding of factor von Willebrand (vWF) to collagen and high molecular weight multimers of vWF according to the manufacturer's instructions (Technoclone, Austria).

Basal level of insulin in blood was measured using standard kit "RIO-INS-PG-125I" by radioimmunoassay. Glucose level was determined in blood using glucose oxidase.

Soluble fibrin (SF) quantification in human blood plasma was performed by double-sandwich ELISA. Monoclonal antibody FnI-3C was proposed to use as a "catch"-site in ELISA by team of investigators from the Palladin Institue of Biochemisty of the National Academy of Sciences of Ukraine.

Platelet aggregation (PA) by various inductors was studied using the Born spectrophotometric method at aggregometer "Thromlite". Such inductors of aggregation as adenosine 5-diphosphate (ADP) disodium salt in concentration $2.0 \cdot 10^{6}$ M ("Sigma-Aldrich"/"Merck", Canada), collagen in dilution 1:2, ristocetin in concentration 0.8 mg/ml were used.

Blood samples collections as well as measurement of BMI and blood pressure (BP) were provided twice. For the first time, data was collected immediately after recruitment the patient into the study. Once more, data was collected after 12 weeks of standard therapy (I group) or standard therapy in combination with carbohydrate restricted diet (II group).

Statistical analyses were done using "Stata-12". Numerical variables were presented as mean±standard deviation (SD) for normal type of distribution. Student t-test was used for comparisons of independent samples. Paired t-test was used for paired samples. P value < 0.05 was considered statistically significant. Categorical variables are presented as absolute numbers and percentages.

Results of the study and their discussion. Baseline characteristics of patients are shown in table 1. The results have shown no significant difference in the characteristics of patients of both groups under investigation.

Table 1

Baseline demographics, clinical and biochemical characteristics

Characteristic	Group I (n=26)	Group II (n=24)	P value
Age, Years	62.5±4.3	59.4±3.9	0.46
Male, % (n. / total)	42 (11/26)	41 (10/24)	0.54
History of AH, Years	5.5±2.5	4.7±2.2	0.34
BMI, kg/m^2	29.1±2.8	29.9±2.5	0.59
History of SA FC II-III, % (n./total)	23 (6/26)	21 (5/24)	0.52
History of DM II, % (n./total)	8 (2/26)	8 (2/24)	0.49
SBP, mmHg	164.2±3.2	165.6±4.4	0.44
DBP, mmHg	97.4±5.2	99.2±5.3	0.42
Fasting blood glucose, mmol/l	5.5±0.3	5.4±0.4	0.39
Basal insulin, mmol/l	266.2±32	276.1±35	0.23
vWF, IU/l	0.65±0.17	0.71±0.19	0.19
PA-ADP, %	33.2±4.4	31.3±3.5	0.37
PA-collagen, %	40.7±3.9	43.2±4.7	0.33
PA-ristocetin, %	32.3±2.2	30.6±3.1	0.29
SF, mcg/ml	1.56±0.4	1.62±0.36	0.23

Statistically significant trends of BP normalization were in both groups after course of treatments (table 2).

Table 2

Trends in blood pressure in research groups

Characteristic	Group I (n=26)			Group II (n=24)		
	Before treatment	After treatment	P value	Before treatment	After treatment	P value
SBP, mmHg	164.2±3.2	141.4±3.6	0.0021	165.6±4.4	139.6±3.5	0.0011
DBP, mmHg	97.4±5.2	85.9±2.6	0.0048	99.2±5.3	84.6±2.2	0.0059

Dynamics of BMI, level of fasting blood glucose, level of basal insulin in patients of both groups before and after treatment are shown in table 3. There were no statistically significant changes of BMI in both research groups. Decrease in basal insulin level by 27.8% was showed in group II after following of diet with carbohydrate restriction.

Table 3

Dynamics of BMI, fasting blood glucose, basal insulin n research groups

Parameter	Group I (n=26)			Group II (n=24)		
	Before treatment	After treatment	P value	Before treatment	After treatment	P value
BMI, kg/m^2	29.1±2.8	28.3±2.5	0.47	29.9±2.5	27.4±0.89	0.16
Fasting blood glucose, mmol/l	5.5±0.3	5.2±0.2	0.38	5.4±0.4	4.6±0.2	0.11
Basal insulin, mmol/l	266.2±32.1	242±25.4	0.14	276.1±35.5	199±15.5	0.03

It was found that following the diet with carbohydrate restriction up to 250 g daily for 12 weeks changed some parameters of hemostasis (table 4). It was revealed decrease in level of vWF after treatment course (0.32±0.13 IU/ml vs 0.71±0.19 IU/ml. p=0.009), whereas there were no statistically significant changes of vWF in group I. Statistically significant improvement of PA-ADP after course of treatment was noticed in both groups (41.4±2.1% vs 33.2±3.4% and 40.5±3.4% vs 31.3±3.5%, p=0.02 and p=0.01, respectively), while no significant changes were in PA-collagen. It was found statistically significant normalization of AP-ristocetin as well as decrease in SF only in group II.

Table 4

Trends of hemostasis before and after treatment in research groups

Parameter	Group I (n=26)			Group II (n=24)		
	Before treatment	After treatment	P value	Before treatment	After treatment	P value
vWF, IU/l	0.65±0.17	0.45±0.1	0.13	0.71±0.19	0.32±0.13	0.009
PA-ADP, %	33.2±3.4	41.4±2.1	0.02	31.3±3.5	40.5±3.4	0.01
PA-collagen,%	40.7±3.9	42.3±4.6	0.16	43.2±4.7	45.5±4.6	0.15
PA-ristocetin, %	32.3±2.2	33.5±3.1	0.36	30.6±3.1	37.4±2.1	0.01
SF, mcg/ml	1.26±0.4	1.03±0.3	0.28	1.32±0.36	0.77±0.21	0.03

Most studies dedicated to the carbohydrate-restricted diet explore its input on carbohydrates and lipids metabolism, weight, blood pressure. A carbohydrate-restricted diet is recommended not only for the management of the patients with diabetes mellitus but also for the treatment and prevention of prediabetes, obesity [5].

Thus, the decline in basal insulin level leads to the improvement of insulin influence on the endothelium. It is well-known that insulin as a hormone stimulates the activity of the sympathetic nervous system, cardiac output, BP [8], and has direct atherogenic activity: cause set of hemodynamic and metabolic changes. Such alterations may provoke complications as a result of coagulation disorders [6]. Consequently, the correction of the basal insulin level plays a key role in the prevention and slowing-down of atherosclerosis and its complications [10]. Bando H. et al. registered a remarkable decrease in pre-prandial and postprandial glucose levels in patients following a low carbohydrate diet which suggests the hypoglycemic effect of a carbohydrate-restricted diet. However, we haven't registered a significant decrease in fasting glucose levels. This fact may be connected with the observation that the higher glucose level is the more intensive glucose decreasing effect of carbohydrate-restricted diet is [11].

Meng Y. et al. in the meta-analysis reported the more intensive reduction in weight in patients with diabetes mellitus following a low-carbohydrate diet [12]. In our research, we have registered no significant decrease in BMI in group 2 which may be connected with a limited number of patients as well as the time of observation. However, the trend of its reduction was higher in patients following a carbohydrate-

restricted diet than the standard one. It must be added that Kelly T. et al. in the review suggests studies devoted to diets effect have some potential for bias, residual confounding, and type 1 errors [13].

Though the nutrients influence all three components of the hemostasis to a great extent [14] the data regarding carbohydrate-restricted diet is limited as mostly investigators pay more attention to the unhealthy properties of high-fat diet [5], advantages of the Mediterranean diet and DASH-diet or effects of specific products regarding hemostasis [15].

VWF is a marker of endothelium activation. VWF becomes activated after endothelium damage and the detection of endothelial cell adhesion molecules on the surface of endotheliocytes. VWF facilitates platelet adhesion to vessel wall in the damaged place as the bridge between subendothelial structures of damaged vessel wall and platelets as well as interplatelets bridge. Thrombocyte becomes activated after adhesion, gain the ability to bind vWF, fibrinogen with further promotion of platelets activation process. Thus, vWF stimulates thrombogenesis [9].

The platelets aggregation inductors (ADP, collagen) affect platelets intensively, change its functional ability. As a result, the risk of vascular complications is extremely elevated [15].

VWF activity was decreased and platelet aggregation with ADP and ristocetin was improved significantly in patients of group II (after carbohydrate restriction diet within 12 weeks), whereas the only positive trend in ADP-induced platelets aggregation was registered in group I.

Probably, a decline in vWF activity is connected with normalization of endothelial function after a decrease in basal insulin level and its impact on the endothelium [7]. It was demonstrated a positive influence of additional treatment with carbohydrate restriction on platelet aggregation which stabilizes vascular hemostasis [9].

The decrease in the SF level was registered after treatment in group II. SF represents the appearance of thrombin in the bloodstream which means activation of thrombogenic activity of blood. The decline in SF in patients of group II reflects the general reduction of coagulation abilities of blood and activation of fibrinolysis.

The main study limitation is rather small number of patients. However, this fact is connected with the relatively small compliance of patients to the following of the diet with carbohydrate restriction. Consequently, some of them were excluded from the study.

Conclusions

1. A carbohydrate-restricted diet up to 250 g per day within 12 weeks helps to decrease BMI and basal level of insulin.

2. Such changes as normalization of vWF, PA-ADP, PA-ristocetin, SF reflects the process of vascular hemostasis stabilization and, as a consequence, high effectiveness of such therapy.

3. A carbohydrate-restricted diet should be recommended to the patients with AH in combination with increased BMI and hyperinsulinemia.

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Реферати

ДІЄТИЧНА КОРЕКЦІЯ ГІПЕРІНСУЛІНЕМІЇ, ПОКАЗНИКІВ ГЕМОСТАЗУ У ХВОРИХ НА АРТЕРІАЛЬНУ ГІПЕРТЕНЗІЮ З ПІДВИЩЕНОЮ МАСОЮ ТІЛА

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Метою дослідження було вивчити вплив дієти з обмеженням вуглеводів до 250 г на добу впродовж 12 тижнів на індекс маси тіла, рівень інсуліну, показники гемостазу у хворих на артеріальну гіпертензію з метаболічними розладами. Терапія з обмеженням вуглеводів дала змогу у хворих основної групи знизити ІМТ на 7%, рівень інсуліну на 27.8%, достовірно покращити АДФ-індуковану та ристоцетин-індуковану агрегацію тромбоцитів, знизити активність фактора фон Віллебранда (p=0.009) і вміст розчинного фібрину (p=0.03). Доцільно рекомендувати гіповуглеводну дієту з обмеженням вуглеводів до 250 г на добу хворим на артеріальну гіпертензію з підвищеною масою тіла та гіперінсулінемією разом з антигіпертензивною терапією.

Ключові слова: артеріальна гіпертензія, гіповуглеводна дієта, індекс маси тіла, рівень інсуліну, показники гемостазу.

Стаття надійшла31.08.2019 р.

ДИЕТИЧЕСКАЯ КОРРЕКЦИЯ ГИПЕРИНСУЛИНЕМИИ, ПОКАЗАТЕЛЕЙ ГЕМОСТАЗА У БОЛЬНЫХ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ С ПОВЫШЕНОЙ МАССОЙ ТЕЛА

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Целью исследования было изучить влияние диеты с ограничением углеводов до 250 г в сутки в течение 12 недель на индекс массы тела, уровень инсулина, показатели гемостаза у больных АГ с метаболическими нарушениями. Проводимая терапия у больных основной группы дала возможность снизить индекс массы тела на 7%, уровень инсулина на 27.8%, достоверно улучшить АДФ-индуцированную и ристоцетин-индуцированную агрегацию тромбоцитов, снизить активность фактора фон Виллебранда (p=0.009) и содержание растворимого фибрина (p=0.03). Гипоуглеводная диета с ограничением углеводов до 250 г в сутки должна рекомендоваться больным АГ с повышеной массой тела и гиперинсулинемией наряду с антигипертензивной терапией.

Ключевые слова: артериальная гипертензия, гипоуглеводная диета, индекс массы тела, уровень инсулина, показатели гемостаза.

Рецензент Катеренчук І.П.

DOI 10.26724/2079-8334-2020-3-73-69-74
UDC 616.31.17:616.89-053.81

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THE EFFECT OF THE PSYCHO-EMOTIONAL STRESS ON THE STATE OF MICROBIOTA OF THE GINGIVAL SULCUS

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This study aimed to investigate the effect of psycho-emotional stress on the state of microbiota of the gingival sulcus in the state of eubiosis and dysbiosis in young people. The research involved 182 students of the medical university. As a model of acute psycho-emotional stress the situation of passing an important exam was used. A microbiological examination of the total microbial population of gingival sulcus and its population of microbiota, was performed with the standard methods. The impact of the stressor on the background of imbalance of the microbial homeostasis of the tooth-gingival crevice, causes the intensification of the imbalance of microbial associations in the form of commensal microflora reduction and the increase of opportunistic microflora.

Keywords: microbiota of the gingival sulcus, eubiosis, dysbiosis, psycho-emotional stress.

The work is a fragment of the research project "Study of the role of opportunistic and pathogenic infectious agents with different sensitivity to antimicrobial antiviral drugs in human pathology», state registration No. 0118U004456.

The complex of symbiotic microorganisms, that inhabit the open biotope of a macroorganism, make up its microbiome, provide a colonization resistance and have a great impact on the health and development of pathological processes in the human body. [4, 5, 8, 9].

The oral cavity has one of the most diverse microbiome in the human organism, which includes bacteria, fungi, protozoa and viruses. The uniqueness of the biotope of the gingival sulcus lies in the fact that quantitative and qualitative changes of microbial communities (dysbiosis) of this micro-ecological system can lead to major dental diseases such as: gingivitis, periodontitis and caries. Structural and