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КОРРЕКЦИЯ МЕТАБОЛИЧЕСКОГО ПРОФИЛЯ ПАЦИЕНТОВ С ОБСТРУКТИВНЫМ АПНОЭ СНА В ЗАВИСИМОСТИ ОТ ДЛИТЕЛЬНОСТИ СЕАНСОВ CPAP-ТЕРАПИИ

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Metabolic Profile Correction in Patients with Obstructive Sleep Apnea Depends on the Duration of CPAP Therapy Sessions

Резюме

Обструктивное апноэ сна (ОАС) является распространённым гетерогенным хроническим заболеванием с фрагментацией сна, метаболическими и сердечно-сосудистыми нарушениями. Терапия постоянным положительным воздухоносным давлением (CPAP-терапия) служит основным методом лечения пациентов ОАС. Однако, воздействие длительно проводимой CPAP-терапии с ночными сеансами более 6 часов остается малоизученным. Целью исследования явилось изучение эффектов различной длительности ночных сеансов CPAP-терапии на «метаболический профиль» пациентов с тяжёлым течением ОАС. **Материалы и методы.** В ретроспективное исследование «случай-контроль» сравнения двух режимов CPAP-терапии путём подбора пар из числа пациентов с верифицированным тяжёлым ОАС (индекс апноэ-гипопноэ >30/ч), артериальной гипертензией, ожирением I-II степени по классификации ВОЗ (1997), подписавших информированное согласие, были сформированы две группы по 18 человек в каждой, сопоставимые по возрасту, антропометрическим и сомнографическим показателям, использующие CPAP-терапию 4-6 ч/ночь и более 6 ч/ночь соответственно. Пациенты получали CPAP-терапию в течение года, визиты осуществлялись на 3, 6 и 12 месяцы. Характер и тяжесть апноэ сна верифицировалась в ходе ночной компьютерной сомнографии (КСГ) на аппаратном комплексе WatchPAT-200 (ItamarMedical, Израиль) с оригинальным программным обеспечением zzzPAT™SW ver. 5.1.77.7 (ItamarMedical, Израиль) путём регистрации основных респираторных полиграфических характеристик в период 23:00 — 7:30. Оптимальный лечебный уровень CPAP-терапии титровался в домашних условиях с использованием аппаратов для автоматического выбора лечебного давления («PR System One REMstar Auto CPAP Machine with A-Flex» (Philips Respironics, США)) в течение 7 дней после диагностического исследования. Для оценки показателей комплаенса пациентов использовалось оригинальная программа анализа комплаентности Encore Pro v.2.14 (Philips Respironics, США). **Результаты.** При исходной сопоставимости групп уже к 3-му месяцу терапии пациенты группы CPAP >6 ч/ночь демон-

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стрировали статистически значимое преимущество перед пациентами группы с сеансами 4-6 ч по показателям сонливости (ESS), окружности шеи и тестостерона. К 6-му месяцу в группе CPAP >6 ч/ночь возникали статистически значимые различия групп по индексу массы тела, индексу висцерального ожирения, пероральному глюкозотолерантному тесту, индексу инсулинорезистентности, показателям липидного обмена (липопротеиды высокой и низкой плотности, триглицериды, Апо-В), лептина, инсулина натощак. К 12-му месяцу терапии группа CPAP >6 ч/ночь имела улучшение показателей по окружности талии, глюкозы крови натощак и мочевой кислоты. Возникшие различия между группами сохранялись на протяжении всего периода терапии. **Выводы.** Длительно (в течение 12 мес.) проводимая в домашних условиях CPAP-терапия сеансами >6 ч/ночь имеет преимущество над терапией с сеансами 4-6 ч/ночь в достижении более быстрого, выраженного и клинически значимого улучшения показателей метаболического профиля и гормонального фона у пациентов ОАС тяжёлого течения.

Ключевые слова: *обструктивное апноэ сна, ОАС, CPAP-терапия, WatchPAT-200, компьютерная сомнография, КСГ, метаболический профиль, гормональный фон*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

Obstructive sleep apnea (OSA) is a common, heterogeneous chronic disease with sleep fragmentation, metabolic and cardiovascular disorders. Continuous Positive Air Pressure (CPAP) therapy is the primary treatment for patients with OSA. However, the effects of long-term CPAP therapy with night sessions > 6 hours remain poorly understood. The aim of the study was to study the effects of different durations of night sessions of CPAP therapy on the "metabolic profile" of patients with severe OSA. **Materials and methods.** In a retrospective case-control study comparing two CPAP-therapy regimens by matching pairs from among patients with verified severe OSA (apnea-hypopnea index> 30/h), arterial hypertension, obesity of I-II degrees according to the WHO classification (1997), signed informed consent, 2 groups of 18 people each were formed, comparable in age, anthropometric and somnographic indicators, using CPAP therapy 4-6 hours / night and more than 6 hours / night, respectively. Patients received CPAP therapy for a year, visits were carried out at 3, 6 and 12 months. The severity of sleep apnea was verified during nighttime computed somnography (CSG) on WatchPAT-200 hardware (ItamarMedical, Israel) with original software zzzPAT™SW ver. 5.1.77.7 (ItamarMedical, Israel) by registering the main respiratory polygraphic characteristics from 11.00 PM to 7:30 AM. The optimal therapeutic level of CPAP therapy was titrated at home using devices for automatic selection of therapeutic pressure (PR System One REMstar Auto CPAP Machine with A-Flex (Philips Respironics, USA)) within 7 days after the diagnostic study. To assess the compliance of OSA patients at 3-6-12 months of CPAP-therapy, we used the original compliance analysis program Encore Pro v.2.14 (Philips Respironics, USA). **Results.** With the initial comparability of the groups, by the 3rd month of therapy, patients with CPAP > 6 h/night showed a statistically significant advantage over the patients with 4-6 h CPAP-therapy in ESS, neck circumference and testosterone. By the 6th month, statistically significant differences of BMI, VAI, leptin, oral glucose tolerance test, fasting insulin, HOMA-IR, lipid metabolism (HDL, LDL, triglycerides, Apo-B) appeared. By the 12th month of therapy, the CPAP group > 6 h/night had a statistically significant advantage in waist circumference, fasting blood glucose and uric acid. Differences between groups at control points persisted throughout the observation period. **Conclusions.** Long-term home-based CPAP therapy with sessions > 6 h/night has an advantage over therapy with sessions 4-6 h/night in achieving a rapid and pronounced improvement in metabolic profile and hormonal levels in patients with severe OSA.

Key words: *obstructive sleep apnea, OSA, CPAP-therapy, WatchPAT-200, computer somnography, CSG, metabolic profile, hormonal levels*

Conflict of interests

The authors declare no conflict of interests

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AHI — apnea-hypopnea index, BMI — body mass index, BP — blood pressure, CPAP — constant positive air pressure, DI — desaturation index, ESS — Epworth Sleepiness Scale, GCP — good clinical practice, HDL — high-density lipoproteins, HOMA-IR — insulin resistance index, HR max — maximum night heart rate, HR min — minimum night heart rate, LDL — low density lipoproteins, NSG — night somnography, NC — neck circumference, OGTT — oral glucose tolerance test, OSA — obstructive sleep apnea, REM sleep — rapid eye movement sleep, SpO_2 mean — mean night saturation, SpO_2min — minimum night saturation, STOP-BANG — obstructive sleep apnea marker scale, TSat90 — time at saturation less than 90%, URT — upper respiratory tract, WC — waist circumference

Introduction

Obstructive sleep apnea (OSA), a common heterogeneous chronic disease with cyclic respiratory pauses (apnea) and nocturnal hypoxemia/desaturation, is characterized by sleep fragmentation, excessive daytime sleepiness (EDS), and metabolic and cardiovascular disorders [1, 2]. Also, OSA is directly associated with an increased risk of fatal and nonfatal cardiovascular complications (CVC) [2, 3]. Continuous positive airway pressure (CPAP) therapy is the main treatment method for patients with OSA of different severity. Compliance with the CPAP therapy regimen is critical for patients with OSA in improving their quality of life, controlling blood pressure (BP), and eliminating EDS [4]. An analysis of 82 randomized clinical trials (RCTs) by Rotenberg B.W. et al. (2016) showed that non-compliance with the CPAP therapy regimen reduced its effectiveness in 1/3 of treated patients with OSA. Compliance with treatment was low in patients with OSA who had minimal severity of symptoms, heterogeneous metabolic disorders, or comorbidities in the form of neurological disorders [5]. Paradoxically, most RCTs were performed in patients with moderate OSA, on CPAP therapy for no more than three months, without assessing the "metabolic profile" even in the presence of carbohydrate and lipid metabolism disorders [6]. Our study sought to analyze the "metabolic profile" of patients with severe OSA taking into account the duration of night CPAP sessions during 12 months of treatment.

Materials and Methods

Study Design. In a retrospective case-control study for comparing two CPAP therapy regimens by matching pairs from patients with verified severe OSA (apnea-hypopnea index > 30/h), arterial hypertension, obesity of grade I-II according to the WHO classification (1997), who signed informed consent, two groups were formed, each with 18 subjects, comparable in age, anthropometric and somnographic parameters; using CPAP therapy 4–6 h/night, or more than 6 h/night, respectively. Patients received CPAP therapy for one year; visits were made in 3, 6, and 12 months. The inclusion criteria were the following: 1) males; 2) apnea-hypopnea index (AHI) > 30/h; 3) duration of CPAP therapy > 4 hours/night during one year of follow-up; and 4) signed informed consent. Matching of pairs of patients was performed according to the following criteria: 1) age ±5 years; 2) BMI ±1 kg/m^2; 3) neck circumference (NC) ±1 cm; 4) AHI ±10/h; 5) desaturation index (DI) ±5 events/hour; 6) time at saturation less than 90% (TSat90) ±5%.

This study was carried out at the Department of Phthisiology and Pulmonology of the Faculty of Medicine of A.I. Evdokimov Moscow State Medical and Dental University (A.I. Evdokimov MSMDU of the Russian Ministry of Health) at the Central Union Hospital of the Russian Federation (Moscow); it met good clinical practice (GCP) standards and the principles of the Helsinki Declaration and was approved by the Interacademic Ethics Committee of A.I. Evdokimov MSMDU. Patients were recruited from 2017 to 2020.

Night Somnography (NSG). To detect obstructive sleep apnea, we performed night somnography using a computer-based somnography (CSG) method based on the technology for determining apnea episodes and their consequences by varying changes in peripheral arterial tone (PAT technology) in accordance with the unified rules and recommendations of the American Academy of Sleep Medicine (AASM) [7, 8]. OSA was found using a WatchPAT-200 portable CSG devicer (ItamarMedical, Caesarea, Israel) with original zzzPAT™SW software, ver. 5.1.77.7 (ItamarMedical, Caesarea, Israel) by measuring the main respiratory polygraphic parameters between 11:00 p.m. and 7:30 a.m. Sleep apnea-hypopnea index (AHI) of more than 30/h corresponded to severe OSA. Assessment of nocturnal oxygen desaturation index (ODI), mean and minimum nocturnal saturation (SpO_2), heart rate (HR), and sleep stages was performed in accordance with international guidelines [9, 10].

CPAP Therapy. The optimal therapeutic level of CPAP was titrated at home using devices for automatic selection of therapeutic pressure (PR System One REMstar Auto CPAP Machine with A-Flex (Philips Respironics, USA)) within 7 days after the diagnostic study. To assess the compliance parameters of patients with OSA at months 3–6–12 of CPAP therapy, we used the original compliance analysis software Encore Pro v. 2.14 (Philips Respironics, USA). The main analyzed parameter was the duration of the night session of CPAP therapy with the function of auto-adaptation to the patient's inspiration and expiration (A-Flex); according to this parameter, the patients were divided as: 1) low-compliant < 4 h/night; 2) medium-compliant—4–6 h/night; 3) highly compliant > 6 h/night [11].

Laboratory Tests. Venous blood sampling was carried out in the morning, in a fasting state, after 12 hours of fasting. Laboratory tests were standardized and were carried out on the same laboratory equipment using INVITRO reagent kits for the determination of total cholesterol (TC), low (LDL) and high-density lipoproteins (HDL), triglycerides, uric acid, apolipoprotein B (Apo-B), C-reactive protein (CRP), leptin, testosterone, insulin, and glucose— in a fasting state and 2 hours after the standard oral glucose tolerance test (OGTT). HOMA-IR index was calculated using the following formula: fasting

glucose (mmol/L) × fasting insulin (μU/mL)) ÷ 22.5. Sensitivity to insulin was considered to be within the normal range at HOMA-IR value ≤ 2.77.

Statistical Analysis. Statistical data analysis was carried out using commercial software packages STATISTICA 13.0 (TIBCO Software Inc., USA) and PASW Statistics v.18 (IBM, USA). The distributions of quantitative and qualitative ordinal characteristics (with more than 5 ranks) are represented by medians (Me) and quartiles (lower, Q1, and upper, Q3); qualitative characteristics—in the form of the absolute number of observations (n) and the percentage (%) of the total number of patients in the group. Pairwise comparison of unrelated groups in terms of quantitative and qualitative ordinal (with more than 5 ranks) characteristics was carried out using the nonparametric Mann–Whitney test. The threshold level of statistical significance was considered to be 0.05; for multiple comparisons, the Bonferroni correction was applied.

Results

Intergroup comparison of the parameters of the "metabolic profile" (anthropometric, metabolic, hormonal) before starting CPAP therapy showed the comparability of groups (Table 1).

Further, the groups were compared according to the studied parameters at three subsequent visits.

Таблица 1. *Характеристика групп пациентов до начала терапии*
Table 1. *Baseline patients' parameters*

Parameter	CPAP 4-6 hrs (n=18)	CPAP >6 hrs (n=18)	P, Mann-Whitney test
Age, yars	47 [43; 50]	46 [43; 47]	0,45
BMI, kg/m^2	34,35 [31,6; 35,5]	33,1 [32,2; 35,3]	0,54
Neck circumference, cm	44,8 [43,5; 45,5]	45,0 [44,0; 45,5]	0,65
Waist circumference, cm	111,75 [107; 117]	111,75 [108; 115]	0,70
Epworth sleepiness scale (ESS), score	12 [9; 12]	12 [12; 13]	0,22
Visceral Adiposity Index, (VAI)	3,21 [2,98; 3,58]	3,3 [2,81; 3,49]	0,96
Computer somnography data			
Apnoea-hypopnea index (AHI) (h^{-1})	50,2 [38,4; 56,2]	50,1 [39,4; 54,68]	0,87
Oxygen desaturation index (ODI), (h^{-1})	38,25 [24,1; 51,3]	39,2 [21,2; 47,1]	0,55
Percentage of time with oxygen saturation < 90%, (TSat90), %	23,0 [15,2; 29,1]	23,75 [5,2; 37,0]	0,95
SpO_2 mean, %	91,0 [89,0; 92,0]	91,5 [89,0; 94,0]	0,42
SpO_2min, %	76,5,0 [73,0; 81,0]	73,5 [66,0; 83,0]	0,41
HR min, min^{-1}	46,5 [45,0; 48,0]	46,5 [43,0; 50,0]	0,99
HR max, min^{-1}	101,5 [94,0; 108,0]	101,0 [99,0; 102,0]	0,43
REM sleep, %	15,0 [13,6; 26,5]	14,6 [13,3; 20,4]	0,53
Light sleep, %	74,4 [59,3; 80,65]	75,7 [60,6; 81,1]	0,66
Deep sleep, %	10,0 [6,03; 13,5]	7,6 [6,2; 11,6]	0,95
Laboratory data			
Fasting blood glucose, mmol/l	5,6 [5,4; 5,9]	5,6 [5,4; 5,8]	0,75
Oral glucose tolerance test, mmol/l	7,2 [6,2; 8,0]	7,4 [6,0; 8,0]	0,90
Fasting insulin, μU/ml	16,9 [14,5; 20,3]	18,4 [15,3; 19,8]	1,00
HOMA-IR	4,5 [3,52; 5,14]	4,77 [3,6; 5,04]	0,96
HDL, mmol/l	0,98 [0,92; 0,99]	0,95 [0,91; 1,0]	1,00
LDL, mmol/L	3,49 [3,09; 3,72]	3,43 [3,11; 3,71]	0,91
Triglycerides, mmol/L	2,29 [2,16; 2,42]	2,16 [2,11; 2,42]	0,48
Apolipoprotein B, g/L	1,3 [1,26; 1,34]	1,36 [1,24; 1,44]	0,14
Uric acid, μmol/L	452,5[430,0;471,0]	460,5[432,0;470,0]	0,65
Testosterone, nmol/l	7,93 [7,1; 8,79]	8,13 [7,44; 8,72]	0,41
Leptin, ng/ml	25,1 [19,8; 32,6]	27,7 [22,5; 34,5]	0,99

Note: data are presented as medians and quartiles, Me [Q1; Q3]

Clinical and Anthropometric Parameters

Comparison of patients of the studied groups in terms of sleepiness (ESS) and neck circumference shows a statistically significant difference by month 3 (Table 2).

A clinically and statistically significant advantage of CPAP > 6 h/night compared to 4–6 h sessions was observed at Month 6 in terms of BMI and VAI, and at Month 12 of therapy—in terms of decreased waist circumference. Differences between the groups that arose at the control points persisted throughout the follow-up period. Established patterns indicate the advantage of CPAP > 6 h/night in improving anthropometric parameters and reducing the volume of visceral fat.

Laboratory Parameters of Metabolic Disorders

The comparison of patients of the studied groups in terms of carbohydrate, lipid, purine metabolism, and hormonal levels is presented in Table 3.

A clinically and statistically significant advantage of CPAP > 6 h/night before shorter sessions was observed as early as Month 3, in terms of testosterone; at Month 6, in terms of OGTT, HOMA-IR, lipid metabolism parameters (HDL, LDL, triglycerides, Apo-B), leptin, and fasting insulin; at Month 12, in terms of uric acid. Differences between the groups that arose at the control points persisted throughout treatment. The patterns established indicate the advantage of CPAP > 6 h/night in improving the "metabolic profile" and hormonal levels in patients with OSA.

Results and Discussion

CPAP therapy, the first-line therapy for patients with moderate and severe OSA, is deemed capable of effectively eliminating sleep disorders, nocturnal hypoxemia, and excessive daytime sleepiness (EDS). Also, CPAP therapy has a positive effect on the activity of the sympathetic nervous system and renin-angiotensin-aldosterone system (RAAS), which is closely related to the overall energy balance [12]. However, a contradiction was found: patients with OSA either lost weight [13] or did not [14]. A meta-analysis conducted by Drager LF et al. (2015) included 25 RCTs summarizing data on 3,181 patients with OSA who did not use CPAP therapy for more than three months. This study demonstrated the possibility of a slight increase in BMI and body weight in such patients in connection with CPAP therapy, which could worsen "cardiometabolic health" with prolonged (more than six months) use of respiratory support [15]. Results of our study of the positive effect of one-year CPAP therapy on the metabolic profile of patients with severe OSA contradict previous data [15]. However, they are fully in line with the results of recent studies that showed that the duration of night sessions of CPAP therapy is an important prognostic factor of a positive effect on the metabolic profile of

Table 2. *Comparison of clinical and anthropometric parameters of OSA patients on CPAP therapy*

Parameter	Study group / P, test Mann-Whitney	3 months	6 months	12 months
Сонливость (ESS), points	CPAP 4-6 ч. (n=18)	9,5 [8; 11]	8 [7; 8]	7 [7; 8]
	CPAP >6 ч. (n=18)	7,5 [7; 9]	5 [4; 6]	3 [2; 5]
	P	**0,0068**	**<0,0001**	**<0,0001**
BMI, kg/m^2	CPAP 4-6 ч. (n=18)	34,3 [31,6; 35,5]	33,6 [31,1; 34,7]	32,7 [30,7; 34,1]
	CPAP >6 ч. (n=18)	32,3 [31,6; 34,0]	30,7 [29,4; 32,5]	29,1 [27,7; 31,5]
	P	0,11	**0,0075**	**0,0009**
Neck circumference, cm	CPAP 4-6 ч. (n=18)	44,8 [43,5; 45,5]	43,0 [43,0; 45,0]	43,0 [42,0; 44,0]
	CPAP >6 ч. (n=18)	43,0 [43,0; 44,0]	42,5 [42,0; 43,0]	42,0 [42,0; 42,0]
	P	**0,0027**	**0,0025**	**0,0005**
Waist circumference, cm	CPAP 4-6 ч. (n=18)	111,75 [107; 117]	110,0 [104; 116]	109,0 [104; 114]
	CPAP >6 ч. (n=18)	111,0 [107; 114]	108,5 [104; 111]	105,0 [99; 107]
	P	0,45	0,22	**0,02**
Visceral Adiposity Index, (VAI)	CPAP 4-6 ч. (n=18)	3,21 [2,83; 3,58]	2,78 [2,53; 3,24]	2,52 [2,37; 2,89]
	CPAP >6 ч. (n=18)	2,94 [2,54; 3,19]	2,19 [2,01; 2,6]	1,76 [1,57; 1,96]
	P	0,21	**0,0002**	**<0,0001**

Note: data are presented as medians and quartiles, Me [Q1; Q3]

patients with OSA when it is carried out at home for a long time [16–18]. Our study is unique in the establishment of a threshold value for nocturnal respiratory support that lasts more than 6 h/night, which can effectively control and restore the "metabolic profile" of patients with severe OSA. In our opinion, this will allow practitioners to change the treatment strategy of CPAP therapy towards extending its duration and to plan the follow-up of patients with OSA, which can be carried out in an outpatient setting.

Table 3. *Comparison of biochemical parameters of metabolic disorders in OSA patients on CPAP therapy*

Parameter	Study group / P, test Mann-Whitney	3 months	6 months	12 months
Carbohydrate metabolism				
	CPAP 4-6 ч. (n=18)	5,6 [5,4; 5,8]	5,6 [5,4; 5,8]	5,6 [5,4; 5,8]
Fasting blood glucose, mmol/l	CPAP >6 ч. (n=18)	5,6 [5,4; 5,7]	5,5 [5,2; 5,7]	4,95 [4,6; 5,4]
	P	0,45	0,12	**0,0002**
	CPAP 4-6 ч. (n=18)	7,2 [6,2; 8,0]	7,2 [5,9; 8,0]	7,2 [5,9; 7,6]
Oral glucose tolerance test, mmol/l	CPAP >6 ч. (n=18)	7,1 [6,0; 7,7]	5,95 [5,5; 6,5]	5,95 [5,5; 6,2]
	P	0,56	**0,0089**	**0,0034**
	CPAP 4-6 ч. (n=18)	16,2 [14,0; 19,5]	15,0 [12,9; 17,4]	14,2 [12,4; 16,8]
Fasting insulin, μU/ml	CPAP >6 ч. (n=18)	16,2 [12,5; 18,2]	12,5 [10,2; 14,3]	9,4 [8,5; 10,8]
	P	0,34	**0,019**	**<0,0001**
	CPAP 4-6 ч. (n=18)	4,24 [3,42; 4,94]	3,85 [3,01; 4,48]	3,64 [2,88; 4,25]
HOMA-IR	CPAP >6 ч. (n=18)	4,11 [3,06; 4,59]	3,01 [2,42; 3,72]	2,01 [1,72; 2,59]
	P	0,33	**0,02**	**<0,0001**
Lipid metabolism				
	CPAP 4-6 ч. (n=18)	0,98 [0,92; 1,00]	0,99 [0,92; 1,06]	0,99 [0,96; 1,06]
HDL, mmol/l	CPAP >6 ч. (n=18)	0,98 [0,96; 1,07]	1,13 [1,03; 1,17]	1,19 [1,09; 1,24]
	P	0,25	**0,0016**	**<0,0001**
	CPAP 4-6 ч. (n=18)	3,49 [3,08; 3,72]	3,48 [3,05; 3,71]	3,38 [2,98; 3,65]
LDL, mmol/L	CPAP >6 ч. (n=18)	3,33 [3,03; 3,65]	2,9 [2,75; 3,21]	2,58 [2,38; 2,83]
	P	0,57	**0,018**	**0,0003**
	CPAP 4-6 ч. (n=18)	2,25 [2,08; 2,42]	2,04 [1,93; 2,17]	1,86 [1,83; 1,97]
Triglycerides, mmol/L	CPAP >6 ч. (n=18)	2,04 [2,00; 2,34]	1,65 [1,61; 1,85]	1,51 [1,36; 1,57]
	P	0,12	**<0,0001**	**<0,0001**
	CPAP 4-6 ч. (n=18)	1,3 [1,26; 1,34]	1,29 [1,26; 1,33]	1,29 [1,23; 1,33]
Apolipoprotein B, g/L	CPAP >6 ч. (n=18)	1,24 [1,19; 1,32]	1,19 [1,16; 1,26]	1,15 [1,13; 1,18]
	P	0,15	**0,0017**	**<0,0001**
Purine metabolism				
	CPAP 4-6 ч. (n=18)	452,5[427,0;471,0]	438,5[420,0;455,0]	429,5[414,0;448,0]
Uric acid, μmol/L	CPAP >6 ч. (n=18)	452,0[428,0;462,0]	425,0[402,0;429,0]	381,0[361,0;401,0]
	P	0,84	0,053	**<0,0001**
Hormonal levels				
	CPAP 4-6 ч. (n=18)	7,93 [7,1; 8,79]	8,26 [7,61; 9,0]	9,11 [8,22; 10,1]
Testosteron, nmol/l	CPAP >6 ч. (n=18)	9,63 [9,08; 10,68]	14,87 [12,46; 15,89]	19,22 [15,67; 22,17]
	P	**0,0008**	**<0,0001**	**<0,0001**
	CPAP 4-6 ч. (n=18)	24,9 [19,5; 32,6]	23,05 [18,2; 32,0]	23,7 [16,8; 26,7]
Leptin, ng/ml	CPAP >6 ч. (n=18)	26,4 [20,1; 30,5]	19,9 [17,3; 22,6]	12,6 [10,4; 13,6]
	P	0,70	**0,031**	**<0,0001**

Note: data are presented as medians and quartiles, Me [Q1; Q3]

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