

Original article

Periodontal health and cardiovascular risk factors in adolescents with high blood pressure

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Abstract: *Objective* — To establish significant associations between periodontium status, circadian blood pressure (BP) profile and cardiovascular risk factors in adolescents with high BP.

Material and Methods — The cross-sectional study involved 113 adolescents (78 boys) aged 10 to 17 years, with a BP level (during repeated office measurements) of ≥ 95 percentile for age, height and sex, or $\geq 140/90$ mmHg in adolescents older than 16 years. All adolescents were subjected to 24-hour blood pressure monitoring, anthropometric measurements, laboratory blood tests (lipids, uric acid, alanine aminotransferase, aspartate aminotransferase, fasting glucose), echocardiography (left ventricular myocardial mass index, relative wall thickness), assessment of the stage of puberty, dental examination (complex periodontal index (CPI), oral hygiene index). The association between the periodontium status and cardiovascular risk factors was assessed using univariate and multiple regression analysis, adjusted by sex, age, Tanner stage, body mass index, and oral hygiene index.

Results — Clinical features of periodontitis were found in 32.7% of adolescents. Multiple regression analysis showed the presence of significant associations of CPI with the levels of systolic, mean and pulse BP during 24 hours ($\beta=0.42$, $p=0.0001$; $\beta=0.31$, $p=0.003$ and $\beta=0.26$, $p=0.018$, respectively), diastolic BP in the daytime ($\beta=0.23$, $p=0.019$), as well as the indices of load with high systolic BP within 24 hours ($\beta=0.42$, $p=0.0001$) and diastolic BP in the daytime ($\beta=0.25$, $p=0.006$). None of the other cardiovascular risk factors showed meaningful relationships with periodontium status in the multivariate analysis.

Conclusion — The relationship between periodontium status and blood pressure level exists already in adolescence. That may, on the one hand, justify assessment of periodontium status and (if necessary) timely implementation of prophylactic measures in adolescents with high blood pressure and, on the other hand, recommend BP assessment in adolescents with diagnosed periodontitis.

Keywords: hypertension, blood pressure, periodontitis, oral hygiene, ambulatory blood pressure monitoring, adolescents.

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Introduction

41 million people die from non-communicable diseases every year in the world, which accounts for 71% of all deaths. In the structure of this mortality, the largest proportion belongs to cardiovascular diseases (CVD); that is 17.9 million people annually. That is why WHO urges to focus on combating the main risk factors of CVD development, which would prevent about three quarters of cases of myocardial infarctions, strokes and type 2 diabetes mellitus [1].

Hypertension (AH) is one of the key risk factors for CVD. Its prevalence is 30-45% in the adult [2], and on average 11.2% among adolescents [3, 4]. Despite recent years' significant progress in understanding the pathophysiology of this disease and the risks associated with it, as well as appearance of multiple evidences that lowering blood pressure (BP) can greatly reduce premature morbidity and mortality, no country in the world has achieved significant success in the fight against hypertension [2]. One of the reasons for this is the high frequency of comorbidity. The comorbidity of hypertension and, for example, diabetes, chronic kidney disease, obstructive pulmonary disease, has long

been known and is already considered in choosing the approaches to management of hypertension. At the same time, the comorbidity of hypertension and periodontal diseases attracted the attention of researchers only a little more than twenty years ago and, to this point, has not been studied enough [5].

However, periodontitis, along with hypertension, is one of the most common non-communicable diseases. According to epidemiological studies, 49% of the common population suffer from generalized periodontitis and 80-90% of people have mild forms of this disease [6, 7].

By now, researchers established relations of periodontitis to obesity, lipid and carbohydrate metabolism disorders, myocardial infarction and cerebral strokes. In the European Guidelines for CVD Prevention in Clinical Practice (2016), periodontitis, along with chronic kidney diseases, oncological and autoimmune diseases, is classified as a clinical condition that affects cardiovascular risk [8].

Many studies confirm connections between periodontitis and the level of BP and hypertension, which creates prerequisites for substantiating new approaches to CVD prevention, through the

disclosure of mechanisms that mediate the association of these comorbid risk factors. This is especially important in the light of recently published results of the USA National Health and Nutrition Examination Survey (2009 – 2014). It showed that the periodontitis in adult patients with hypertension is associated with a lack of effect from antihypertensive therapy; and, vice versa, good periodontal health is associated with the best systolic BP profile against the background treatment and with lower chances of its inefficiency [9].

However, it should be noted that existing studies do not answer the question “when is the connection between hypertension and periodontitis formed in the process of unfolding the cardiometabolic continuum.” They also do not establish any direction of causality in this association. Longitudinal studies could help in solving this problem, but the clinical course specific for periodontitis (chronic course with periods of exacerbation and more or less long remissions) impedes the tracking of connections between these risk factors, which makes interpret the results of these studies very carefully. One of the justified research approaches may be conducting a research in a cohort of adolescents, since it provides a unique opportunity to study the early pathogenesis of diseases. This is very important because the majority of published works usually include middle-aged and elderly patients, who are burdened with multiple comorbidity, as a rule, which complicates the already complex nature of the relationship between hypertension and periodontal status.

The objective of this study was to establish the presence of significant associations between the periodontal status, the characteristics of daily BP profile and the cardiovascular and cardiometabolic risk factors in adolescents with increased blood pressure.

Material and Methods

Study design

The cross-sectional study was conducted in 2014–2015 at the Scientific Centre for Family Health and Human Reproduction Problems. The study sequentially included adolescents sent to the clinic because of BP level increase detected at outpatient examinations or adolescents with an established hypertension.

The criteria for inclusion to the study were: the age between 10 and 17 years; the BP level during repeated office measurements of ≥ 95 percentile for age, height and sex, or $\geq 140/90$ mmHg in the adolescents older than 16 years [10]. An informed voluntary consent to participate in the study, given by adolescents' parents / legal representatives or by adolescents over 15 years of age, was obligatory.

The criteria of exclusion from the study were: secondary hypertension; severe somatic diseases; anomalies of bite; twisted position of teeth; orthodontic treatment carried out at the time of the study; diabetes mellitus.

Weight and height were measured using a stadiometer and an electronic scale. BMI (kg/m^2) was calculated from height and weight, and BMI Z-scores were calculated to standardize BMI measurements for age and sex. The overweight criterion was BMI Z-scores between 1.0 and 2.0; the obesity criterion was BMI Z-scores ≥ 2.0 .

Blood pressure was measured with an automated blood pressure monitor (Omron Healthcare Co., Ltd, Japan) in the sitting position, using appropriate cuff size, three times with a 2-3 minutes' interval between measurements. The final result was taken as the average of the two last measurements [10].

All patients were examined by a pediatric endocrinologist, who determined the stage of puberty according to the Tanner scale [11].

Daily ambulatory blood pressure monitoring (ABPM) was carried out by the oscillometric method (Oscar 2, SunTech Medical Ltd, USA) with a 15 minutes' interval between BP automatic measurements during the day and 30 minutes' interval – at night. Analysis of the results was carried out without considering the effect of habituation. The information from the patient's diary was used to assess the tolerability of the BP measuring procedure, the presence of complaints and the quality of night sleep. For analyzing the mean values and interpreting the indices of the BP variability, the allowed share of unsuccessful measurements per day was not more than 30%.

Hypertension was verified with the level of systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) for any period of the day above the 95th percentile for age, height and sex, or above 130/80 mmHg for 24h, 135/85 mmHg in daytime, 125/75 mmHg at night [10]. The BP values for any period of the day above the 90th percentile, but below the 95th percentile were regarded as elevated blood pressure. Normal BP levels in AMBP but high BP in office measurements was regarded as white coat hypertension [10].

Echocardiography was performed using a standard protocol (Philips IU-22, the Netherlands). The left ventricle myocardial mass (LVM), the LVM index (g/m^2), and the relative wall thickness (RWT) of the left ventricle were calculated. Left ventricular hypertrophy (LVH) was defined as LVMI or RWT of ≥ 95 percentile for age and sex [12, 13].

Laboratory tests

The determination of fasting blood serum glucose concentration was carried by the glucose oxidase method using the kits Novoglyuk-K, M (Vector-Best, Russia). Serum uric acid, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol (TC), triglycerides (TG) and high-density lipoprotein cholesterol (HDL) were determined by the fermentation colorimetric method (Mindray BS-480, China). Low-density lipoprotein cholesterol levels (LDL) was calculated by the Friedewald formula. Atherogenic coefficient is given by the ratio of non-HDL cholesterol to HDL cholesterol. In determining the threshold levels of lipids and glucose, the authors were guided by the criteria proposed by the IDF pediatric group (2007). The level of total cholesterol was considered as elevated when its content in serum was ≥ 5.2 mmol/l, triglycerides – ≥ 1.7 mmol/l, HDL cholesterol – < 1.03 mmol/l, LDL cholesterol – ≥ 3.36 mmol/l, fasting glucose ≥ 5.6 mmol/l [14].

Oral examination

To assess the periodontal status used the complex periodontal index (CPI) after examination of teeth 16, 11, 26, 31, 36, 46. They gave a numerical scoring of the state of periodontium near the examined tooth on the following scale: 0 – absence of dental plaque and signs of periodontal inflammation; 1 point – any amount of soft white deposit, determined by a probe on the corona surface, in the interdental spaces or in the pre-gingival area; 2 points – bleeding with light probing of the periodontal groove; 3 points – any amount of solid deposits (tartar) in the sub-gingival area of the tooth; 4 points – periodontal pocket, defined by a probe; 5 points – pathological tooth mobility of 2nd or 3d

degrees. If there were several signs of damage – bleeding with light probing and the presence of tartar, a higher score was recorded. The CPI values were calculated by the formula: “CPI = total points / the number of teeth”. The CPI interpretation was as follows: 0.1-1.0 – a risk of the disease; 1.1-2.1 – mild lesion; 2.1-3.5 – moderate degree of injury; 3.6-5.0 – severe damage [15].

Oral hygiene was assessed by the Fedorov – Volodkina hygiene index (HI) modified by Pakhomov, taking into account the plaque area on the vestibular surface of teeth 16, 11, 21, 26, 36, 33, 32, 31, 41, 42, 43, 46. Staining of plaque was carried out with the Schiller – Pisarev solution: 1 point – no plaque detected; 2 points – one fourth of the tooth corona surface is stained; 3 points – one half of the tooth corona surface is stained; 4 points – three fourth of the tooth corona surface is stained. The hygiene index was calculated by the formula: “total points / the number of teeth examined”. The assessment of the oral cavity hygienic state was described using the obtained results: 1.1-1.5 – “good”, 1.6-2.0 – “satisfactory”, 2.1-2.5 – “unsatisfactory”, 2.6-3.4 – “bad”, 3.5-5.0 – “very bad” [15].

Statistical analysis

The statistical analysis was performed using the package IBM SPSS Statistics 21 (USA). The Kruskal-Wallis test was used to assess differences between groups in continuous variables. The chi-square test was used to assess differences among discrete variables. The Newman-Keuls test was used for pairwise comparison of groups under the condition of a normal distribution of the quantitative variable. Univariate and multiple regression analyzes were used to assess the presence of significant associations between variables. The CPI values were taken as a dependent variable. The multiple linear regression models were adjusted by sex, age, puberty stage, BMI Z-scores and oral hygiene index. The table data are presented as mean with standard deviations for normal distribution, and as median with low and upper quartiles if the distribution was different from normal.

Results

The study successively involved a total of 113 adolescents – the patients who met the inclusion criteria and had no exclusion criteria; 79 of them were boys. Based on the dental examination results, all adolescents were divided into three groups depending on the CPI score. The first group consisted of adolescents with healthy periodontium (CPI=0), the second – of adolescents with CPI equal to 1, which was clinically expressed by the presence of plaque in all cases (the risk of periodontitis development). The third group included adolescents with CPI equal to 2-3, which corresponded to mild (bleeding of the gingival margin and supra gingival mineralized dental deposits) and moderate (detected pockets and mineralized subgingival dental deposits in addition to bleeding and presence of mineralized dental deposits) periodontal lesions. Severe periodontitis was not diagnosed in the adolescents involved in this study. Comparative clinical and anamnestic characteristics of the groups are shown in *Table 1*.

It can be noted that adolescents in all groups had a high degree of family burden with hypertension, coronary artery disease, type 2 diabetes and obesity, but there were no significant differences among the groups. The age of hypertension onset and the duration of the disease by the time of the examination was also comparable. The formed groups did not differ in the level of physical development and puberty stage, the level of BP in office

measurements and the frequency of diseases that could affect oral health. It was revealed that the number of girls in the group of adolescents with periodontitis was significantly higher than that in the other two groups.

Obesity was diagnosed in 44 (38.9%) adolescents, overweight – in another 22 (19.5%). Dyslipidemia was detected in 34 (30.1%) adolescents impaired fasting glycaemia – in 9 (8%) patients. Echocardiography revealed left ventricular hypertrophy in 13 (11.5%) adolescents. There were no significant differences in the incidence of separate cardiometabolic and cardiovascular risk factors in adolescents with different periodontal health (*Figure 1*).

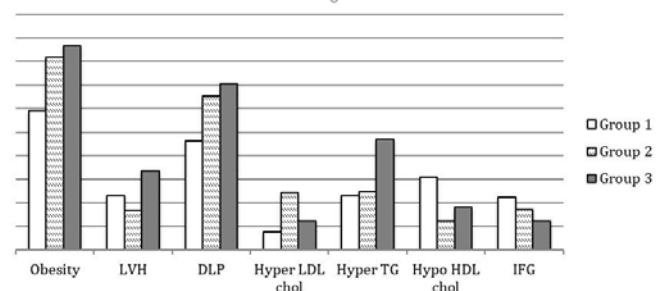


Figure 1. Comparative incidence of separate cardiometabolic and cardiovascular risk factors in the groups of adolescents with different periodontal state. LVH, left ventricular hypertrophy; DLP, dyslipidemia; LDL chol, low density lipoprotein cholesterol; HDL chol, high density lipoprotein cholesterol; TG, triglycerides; IFG, impaired fasting glycaemia.

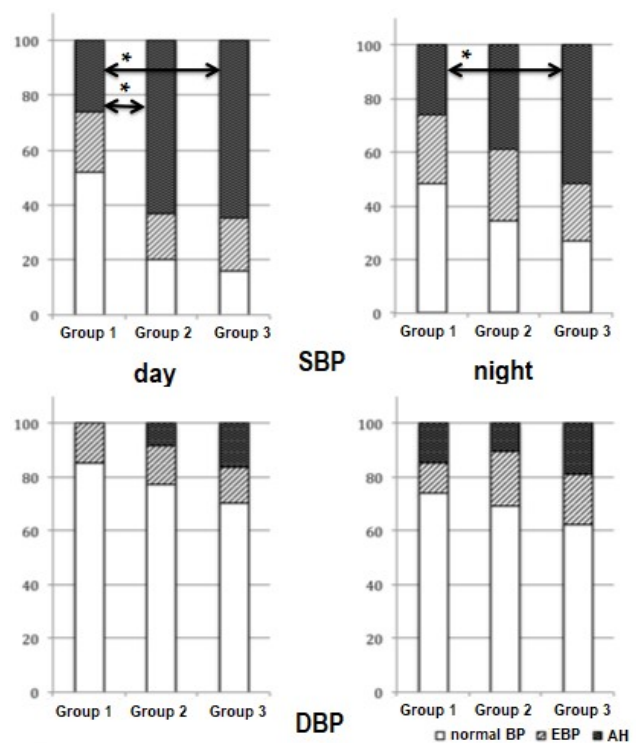


Figure 2. The level of blood pressure during the day in adolescents with different periodontal health, taking into account age, sex and height. EBP, elevated BP; AH, arterial hypertension.

Table 1. Clinical and anamnestic characteristics of adolescents with different periodontal state

| | Group 1 (n=27) | Group 2 (n=49) | Group 3 (n=37) | |
|--|----------------|----------------|----------------|----------------|
| Age, years | 15.1 ± 1.5 | 14.7 ± 2.1 | 14.7 ± 1.7 | p=0.701 |
| Sex – male | 23 (85.2) | 35 (71.4) | 21 (56.8) | p=0.048 |
| Place of residence - city | 22 (81.5) | 36 (73.5) | 29 (77.1) | p=0.827 |
| Family history is burdened with: | | | | |
| - Hypertension | 23 (84) | 36 (73.5) | 28 (75.7) | p=0.593 |
| - CAD | 8 (29.6) | 13 (26.5) | 18 (48.6) | p=0.219 |
| - DM2 | 6 (22.2) | 13 (26.5) | 10 (27) | p=0.941 |
| - obesity | 11 (40.7) | 18 (36.7) | 18 (48.6) | p=0.505 |
| Presence of diseases accompanied with nasal breathing disorder | 2 (7.4) | 7 (14.3) | 6 (16.2) | p=0.569 |
| Chronic tonsillitis | 2 (7.4) | 4 (8.2) | 4 (10.8) | p=0.872 |
| Age of hypertension onset | 13.5±2.2 | 12.7±2.6 | 12.5±2 | p=0.212 |
| Disease duration, years | 1 (0.2; 2) | 1 (0.5; 3) | 2 (1; 3) | p=0.169 |
| Height, cm | 173.4±7.2 | 169.7±12.5 | 170.2±9.1 | p=0.217 |
| Weight, kg | 77.2±21.6 | 74.7±19.6 | 76±17 | p=0.940 |
| BMI, kg/m ² | 25.6±6.7 | 25.6±5.4 | 26.2±5.1 | p=0.655 |
| Height Z-score | 1.6±0.9 | 1.2±1.3 | 1.3±1.1 | p=0.363 |
| BMI Z-score | 1.2±1.4 | 1.4±1.2 | 1.5±1.3 | p=0.696 |
| SBP, mmHg | 128.9±11.7 | 129.7±11.5 | 128.6±8.7 | p=0.982 |
| DBP, mmHg | 73.3±8 | 72.8±10.2 | 74.1±6.6 | p=0.529 |
| Tanner stage: | | | | p=0.132 |
| 1 | 0 | 3 (6.4) | 1 (2.9) | |
| 2 | 1 (3.7) | 3 (6.4) | 1 (2.9) | |
| 3 | 3 (11.1) | 1 (2.1) | 2 (5.8) | |
| 4 | 10 (37) | 18 (38.3) | 18 (52.9) | |
| 5 | 13 (48.1) | 22 (46.8) | 12 (35.3) | |
| Oral hygiene: | | | | 0.175 |
| - Good | 6 (22.2) | 9 (18.4) | 8 (21.6) | |
| - Satisfactory | 12 (44.4) | 22 (44.9) | 11 (29.7) | |
| - Unsatisfactory | 8 (29.6) | 16 (32.6) | 12 (32.4) | |
| - Bad | 1 (3.7) | 2 (4.1) | 6 (16.2) | |

Quantitative data are presented as mean and standard deviation – M±SD, binary variables – as frequencies in absolute values and in percentage – n (%). CAD, coronary artery disease; DM2, type 2 diabetes mellitus; BP, blood pressure; BMI, body mass index; SDS, standard deviation score; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2. The quantitative characteristics of some cardiometabolic and cardiovascular risk factors in adolescents with elevated BP, depending on the periodontal status

| | Group 1 | Group 2 | Group 3 |
|---------------------------|-------------------|-------------------|-------------------|
| LVMM, g | 133 (109, 160) | 127 (103, 146) | 122 (109, 162) |
| LVMMI, g/m ^{2.7} | 31.4±8.2 | 30.1±6.6 | 31.6±7.0 |
| RWT, cm | 0.32±0.04 | 0.32±0.04 | 0.33±0.04 |
| TC, mmol/l | 4.2±0.6 | 4.4±0.8 | 4.2±0.8 |
| HDL chol, mmol/l | 1.4±0.3 | 1.4±0.3 | 1.4±0.2 |
| LDL chol, mmol/l | 2.3±0.5 | 2.5±0.7 | 2.4±0.7 |
| TG, mmol/l | 1.1±0.4 | 1.0±0.3 | 1.1±0.4 |
| Atherogenic coefficient | 2.1±0.8 | 2.1±0.7 | 2.2±0.8 |
| Fasting glucose, mmol/l | 4.9±0.6 | 4.8±0.6 | 5.0±0.5 |
| Uric acid, μmol/l | 356 (318, 406) | 335.3 (273, 397) | 383 (316, 432) |
| ALT, IU/L | 17.5 (13.8, 25.0) | 19.2 (15.5, 24.1) | 20.1 (13.0, 29.3) |
| AST, IU/L | 23.7 (21.4, 26.5) | 25.9 (20.9, 29.3) | 22.0 (19.0, 29.8) |

Quantitative data are presented as mean with standard deviation for normal distribution – M±SD, and as median with low and upper for other types of distribution – Me (LQ, UQ).

LVMM, left ventricle myocardial mass; LVMMI, left ventricle myocardial mass index; RWT, relative wall thickness; TC, total cholesterol; HDL chol, high density lipoprotein cholesterol; LDL chol, low density lipoprotein cholesterol; TG, triglycerides; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

The quantitative characteristics of lipid, carbohydrate and purine metabolism indicators, as well as the levels of hepatic transaminases, were also comparable (Table 2).

According to ABPM, hypertension was verified in 79 (69.9%) adolescents, an elevated BP level – in 13 (11.5%) adolescents and normal daily BP – in 21 (18.6%) adolescents. It was found that in

the group of adolescents with signs of periodontal inflammation, there were significantly more patients with hypertensive levels of SBP in both day and night time ($\chi^2=22.1$, $p<0.001$, and $\chi^2=7.0$, $p=0.030$, respectively) (Figure 2).

The features of the daily BP profile in the studied groups are shown in Table 3.

Monofactorial analysis indicated significant associations of CPI values with average levels of SBP and mBP during 24 hours, DBP and HR at daytime, as well as with indices of load with high 24h SBP and DBP at night (Table 4). In addition, multiple regression analysis showed a significant association between the degree of periodontal damage and pulse BP, but the association of periodontitis with daytime heart rate lost its significance.

None of the other cardiometabolic and cardiovascular risk factors showed significant relationships with periodontal state in the multivariate analysis. The tendency to the presence of a significant association with periodontitis was shown only for fasting plasma glucose ($\beta=0.18$; $p=0.070$).

Discussion

The result of our research showed clinical signs of periodontitis in 32.7% of the adolescents with hypertension. That is higher than the incidence of this disease given in population-based studies (7-24%) [16, 17] and in the study of a selective group of normotensive adolescents (9.2%) [18].

Table 3. The features of the daily BP profile in adolescents with different periodontal state

| | Group 1 | Group 2 | Group 3 | Significance level* |
|-----------------------------|------------|------------|-------------|--------------------------|
| 24 hours | | | | |
| SBP, mm Hg | 127.7±8.3 | 131.8±8.9 | 133.3±8.2 | p ₁₋₃ =0.038 |
| DBP, mm Hg | 70.9±4 | 72.1±5.2 | 73±5.5 | p>0.05 |
| mBP, mm Hg | 89.8±5 | 92.1±5.6 | 93.1±5.5 | p ₁₋₃ =0.062 |
| PBP, mm Hg | 56.9±6.2 | 60.6±8.4 | 60.2±7.3 | p ₁₋₃ =0.103 |
| HR, beats per min | 79.1±12.8 | 80.4±9.6 | 83.1±7.8 | p>0.05 |
| SBP load, % | 33.3±21.4 | 49.2±21.2 | 57.2±21.8 | p ₁₋₂ =0.005 |
| | | | | p ₁₋₃ =0.0002 |
| DBP load, % | 11.8±9 | 20.3±14.6 | 24±16.4 | p ₁₋₂ =0.021 |
| | | | | p ₁₋₃ =0.0003 |
| day | | | | |
| SBP, mm Hg | 130.9±8.2 | 135.5±9.2 | 137±8.1 | p ₁₋₂ =0.04 |
| | | | | p ₁₋₃ =0.021 |
| DBP, mm Hg | 73.4±4.1 | 75.1±5.3 | 76.4±5.9 | p ₁₋₃ =0.070 |
| HR, beats per min | 82.9±11.5 | 84.5±10.2 | 87.5±8.2 | p>0.05 |
| SBP load, % | 36.1±23.0 | 49.4±21.4 | 58.9±22.3 | p ₁₋₂ =0.013 |
| | | | | p ₁₋₃ =0.0002 |
| | | | | p ₂₋₃ =0.073 |
| DBP load, % | 10 (4; 20) | 15 (7; 27) | 17 (10; 35) | p>0.05 |
| night | | | | |
| SBP, mm Hg | 114.3±8.5 | 117.6±8.1 | 119.2±9.7 | p ₁₋₃ =0.085 |
| DBP, mm Hg | 58.8±5.5 | 60.7±6.1 | 60.5±6.4 | p>0.05 |
| HR, beats per min | 62.9±11.2 | 64.6±9.1 | 66.3±9.3 | p>0.05 |
| SBP load, % | 38.1±24.3 | 47.3±25.5 | 55.0±31.7 | p ₁₋₃ =0.028 |
| DBP load, % | 11 (7; 23) | 14 (6; 25) | 14 (5; 50) | p>0.05 |
| nocturnal BP and HR dipping | | | | |
| Systolic dipping, % | 12.3±4.1 | 13.5±5 | 13±4.8 | p>0.05 |
| Diastolic dipping, % | 19.4±5.7 | 20.3±7.4 | 20.5±6.3 | p>0.05 |
| HR dipping, % | 24.8±8.2 | 23.4±7.1 | 24.1±8.2 | p>0.05 |

* using the Kruskal-Wallis test for comparing the three groups and the Newman-Keuls test for pairwise comparison. SBP – systolic BP; DBP – diastolic BP; mBP – mean BP; PBP – pulse BP; HR – heart rate.

In the studied cohort, the frequency of conventional factors of cardiovascular and cardiometabolic risk associated with hypertension was also higher, which is consistent with the results of previous studies [19]. It is noteworthy that, in contrast to the results described in the adult trials, none of these factors demonstrated a significant association with the periodontal state. Meanwhile, such associations were established for the mean daily levels of systolic, mean and pulse BP, the level of DBP in the daytime, as well as for the indices of hypertensive load with SBP and DBP during 24 hours. At that, the worst periodontal state was associated with a higher blood pressure in the daily cycle.

It has been mentioned above that the relationship between periodontal state and BP level was confirmed by a number of studies in the adult cohort [9,20-22]. The number of works focused on studying this problem in young people and adolescents is quite limited. The cross-sectional study of Zeigler et al., which included 75 adolescents with obesity, revealed a significant association between the presence of periodontal pockets ≥4 mm and the level of diastolic BP in office measurements (p=0.008). That corresponds to our conclusion that the connection of periodontitis with BP level appears in early life [23].

In a prospective study that included 4516 students, Kawabata et al. showed that the presence of periodontal pockets with a depth of ≥4 mm and bleeding of gums when probing affects the progression from prehypertension to hypertension within three years of observation, after taking into account the classical cardiovascular risk factors (OR 2.74; 95% CI 1.19-6.29) [24].

Several studies, as well as our work, showed consistent relationships between the BP level and the periodontal state

[20,21]. However, there are works, in which the relationship between the BP level and the presence of severe periodontitis was not found [25].

Such contradictions are apparently caused by significant differences between the studies concerning the populations involved, the list of confounders taken into account, and methodological approaches. Thus, in our work, to characterize individual BP levels, we used the ABPM, the results of which correlate with target organ damage in a best way and have a higher reproducibility than those obtained via office blood pressure [10]. At the same time, the available studies provide the judgments about the presence of hypertension on the basis of office BP measurement results or even from patients' self-reports.

An important result of this study was that the relationship between BP levels and periodontal state obviously does not require severe clinical manifestations for its formation, because none of the adolescents in our study were diagnosed with severe periodontitis. This fact corresponds with the results of a large cross-sectional study conducted in Korea. That study showed a higher risk of hypertension in patients with poor hygienic oral care even before the development of periodontitis [26]. It can be assumed that the realization of periodontal inflammation systemic effects does not always correlate with its local clinical manifestations, but depends on many factors: genetic characteristics, the features of immune reactivity of the host, oral microbiota characteristics, etc. A possible explanation may also be the effect of reverse causality, since most of the pathophysiological links of hypertension are intertwined with the mechanisms of development and progression of periodontal syndrome, and periodontal tissues, along with other target organs, can be included in remodeling processes in the biological scenario of hypertension [27, 28]. It should be noted here that the main scenario of the formation of pathological association between hypertension and periodontitis, which is discussed in the literature, is the development of events from the presence of a chronic inflammatory focus in the periodontium in immunologically and, possibly, genetically predisposed subjects through oxidative stress and endothelial dysfunction to hypertension [28]. There are few research works on reverse causality in the association between periodontitis and hypertension; most of them are experimental ones. Nevertheless, the results obtained in the experiments indicate that hypertensive rats have a worse quality of alveolar bone tissue and adverse morphological changes in the vessels of the gingival and periodontal membrane in the form of hypertrophy of muscular and subendothelial layers of the vascular wall [28, 29].

An unexpected result of our study was that we did not find any association between the periodontal state and the subjects' body mass. Nevertheless, 68% out of 25 studies, which observed the relationship with overweight / obesity in young adults and adolescents, confirmed the existence of such a relationship [30]. Despite the well-known correlation of obesity and hypertension, there are almost no studies devoted to the relationship between the periodontal state and the status of weight, where BP level is taken as a covariate. Thus, it remains unclear how significant becomes the connection between obesity and periodontal state after taking this factor into account. The results obtained by us may be explained by the fact that more than half of adolescents in our study had obesity or overweight. That considerably narrowed the range of BMI Z-scores values and did not allow the possibly existing association to appear in the conditions of small scale this study.

Table 4. Significant and borderline associations between periodontal state and the parameters of daily blood pressure profile in adolescents

| | CPI | | | CPI (adjusted by sex, age, BMI Z-score, Tanner stage, oral hygiene index) | | |
|-----------------|---------|---------------|---------|---|----------------|---------|
| | β | CI | P-level | β | CI | P-level |
| 24h SBP | 0.23 | 0.003 – 0.04 | 0.027 | 0.42 | 0.02 – 0.06 | <0.001 |
| 24h DPB | 0.16 | -0.01 – 0.127 | 0.127 | 0.19 | -0.0002 – 0.07 | 0.063 |
| 24h mBP | 0.22 | 0.002 – 0.07 | 0.039 | 0.31 | 0.02 – 0.08 | 0.003 |
| 24h PBP | 0.13 | -0.01 – 0.04 | 0.204 | 0.26 | 0.005 – 0.05 | 0.018 |
| 24h HR | 0.2 | 0.0001 – 0.04 | 0.051 | 0.14 | -0.01 – 0.03 | 0.196 |
| 24h SBP load | 0.38 | 0.01 – 0.02 | <0.001 | 0.42 | 0.01 – 0.02 | <0.001 |
| 24h DBP load | 0.29 | 0.01 – 0.03 | 0.003 | 0.28 | 0.01 – 0.03 | 0.004 |
| SBP, day | 0.23 | 0.004 – 0.04 | 0.020 | 0.41 | 0.02 – 0.06 | <0.001 |
| DBP, day | 0.2 | 0.0001 – 0.06 | 0.048 | 0.23 | 0.01 – 0.07 | 0.019 |
| HR, day | 0.22 | 0.001 – 0.04 | 0.036 | 0.16 | -0.005 – 0.03 | 0.144 |
| SBP load, day | 0.36 | 0.01 – 0.02 | <0.001 | 0.41 | 0.01 – 0.02 | <0.001 |
| DBP load, day | 0.23 | 0.002 – 0.02 | 0.013 | 0.25 | 0.004 – 0.02 | 0.006 |
| SBP, night | 0.2 | 0.0001 – 0.04 | 0.048 | 0.3 | 0.1 – 0.05 | 0.003 |
| SBP load, night | 0.26 | 0.002 – 0.01 | 0.006 | 0.26 | 0.002 – 0.01 | 0.006 |
| DBP load, night | 0.15 | -0.001 – 0.01 | 0.106 | 0.12 | -0.003 – 0.01 | 0.220 |

95% CI, 95% confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; mBP, mean blood pressure; PBP, pulse blood pressure; HR, heart rate.

Conclusion

The relationship between the periodontal state and the level of blood pressure arises already in adolescence, ahead of the formation of comorbid associations of periodontitis with impaired lipid and carbohydrate metabolism, which are described in the studies of adults. This relationship is consistent in character and appears before the development of severe periodontal disease. The direction of this relationship, as well as the deeper mechanisms underlying it, is not completely clear. Thus, on the one hand, the results obtained in this work substantiate conducting examinations of periodontal state and, if necessary, conducting timely preventive measures in adolescents with an increase in blood pressure. On the other hand, the results give grounds to recommend assessments of blood pressure in adolescents with diagnosed periodontitis. The vector of these activities will be aimed at primary prevention of forming the comorbid associations and reduction of cardiovascular risk in further ontogenesis.

Ethical approval

This study was carried out in accordance with the recommendations set forth in the main document containing the ethical principles of biomedical research involving people, the Helsinki Declaration of the World Medical Association. The study was approved by the Committee on Biomedical Ethics of Federal State Public Scientific Institution «Scientific Centre for Family Health and Human Reproduction Problems» (Record 25.1 as of 8.10.2014).

Conflict of interest: not declared.

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