UNIWERSYTET MEDYCZNY W ŁODZI

WYDZIAŁ LEKARSKI

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Rozprawa na stopień doktora nauk medycznych

„Ocena kompleksu intima-media i wybranych parametrów metabolicznych u pacjentów

z MIZS jako potencjalnych czynników ryzyka rozwoju chorób

układu sercowo-naczyniowego"

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7. Streszczenie pracy w języku angielskim

Introduction

Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children. According to the definition of the International League of Associations for Rheumatology (ILAR), JIA is defined as a heterogeneous group of arthritis that persists for more than six weeks and begins before the age of sixteen. Despite the pursuit toward personalized therapy and access to the latest biologic drugs, the active inflammatory process in about 40% of JIA patients continues well into adulthood. The presence of a chronic inflammatory process and exposure to cardiovascular diseases (CVD) risk factors places children with JIA at moderate risk for the premature development of such diseases and their associated complications. Although CVD is rarely clinically manifested in children, pediatric patients are also at risk of developing CVD. Therefore, it is extremely important to search for diagnostic tools to identify patients at increased exposure to risk factors for developing these conditions. Among the non-invasive methods of assessing the risk of developing CVD is the assessment of the thickness of the common carotid artery intima-media complex (cIMT). It is one of the most well validated methods for assessing the risk of early atherogenesis and thus the occurrence of future cardiovascular events in the general population. However, there are still insufficient studies describing the correlation between cIMT and the impact of exposure to CVD risk factors in the pediatric population of JIA patients, and the results of these studies are inconclusive. Other well-documented atherosclerosis and cardiovascular risk factors also influence the dimension size and progression of cIMT.

Mainly hypertension, but also diabetes mellitus, obesity, nicotinism, lipid disorders, mainly in terms of total cholesterol and triglycerides. Improper diet is also one of the main factors affecting cardiovascular risk directly through physiological, molecular and biological changes related to the initiation of inflammation and oxidative stress. Poor dietary habits may be associated with the development of CVD through negative effects on body weight, blood pressure or lipid profile. Unfortunately, only a few studies raise the issues of the abovementioned correlations, and the results of these studies are often contradictory.

The purpose of the study was:

- to determine the relevance of the cIMT test as a screening test for CVD in patients with JIA,

- to assess the risk factors for CVD in children with JIA,

- to evaluate the relationship between cIMT and selected metabolic parameters in children with JIA,

- to assess the relationship between cIMT and modifiable CVD risk factors (exposure to tobacco smoke, abnormally high total cholesterol, abnormally high blood pressure, abnormal fasting blood glucose, overweight and obesity, insufficient physical activity, incorrect dietary habits),

Material and methods

Publication I

The study group included 386 participants. The study was conducted using an online survey, with a questionnaire available on a closed online forum for mothers who are health care professionals. The questionnaire was anonymous. The questions concerned health-seeking behaviours among

preschool children. The results were subjected to statistical analysis. The data obtained were compared with the results of population studies. The analysed parameters were presented as basic measures of structure description: mean with standard deviation (SD), medians, and structure and intensity indices. The analysed parameters were tested for differences between groups. These differences were checked for statistical significance. The threshold for statistical significance was $p \leq 0.05$. The Student's t-test (for variables following a normal distribution) and the non-parametric U-Mann-Whitney test were applied to verify differences between two groups. To test for differences between more than two groups, one-way analysis of variance ANOVA (for variables following a normal distribution with a normal distribution) and the Kruskal-Wallis test (for non-parametric variables) were applied. Categorical variables were compared using the chi-square or Fischer's test. The normality of the distribution was verified using the Shapiro-Wilk test. The relationship between selected parameters was analysed by calculating Spearman's rank correlation coefficient. Assessment of the differential impact of variables on selected groups was carried out by discriminant analysis using the Wilks Lambda measure. Statistical analysis was performed using Statistica 13 software.

Publication II and III

The study was conducted on a group of 45 patients (33 girls and 12 boys) with a median age of 14.0 (IQR 6.0) years, who were diagnosed with JIA in accordance with ILAR criteria. Eighteen patients were classified as the oligoarticular type, nine as the type with enthesitis-related arthritis (ERA), and the remaining 18 as other subtypes, including systemic JIA, as well as RF-negative and RF-positive polyarticular JIA. Thirty-seven patients, selected by age and sex, were included in the comparison group. These were patients qualified to participate in the study among the Department's patients hospitalized due to cardiovascular disorders, such as syncope. Anthropometric parameters, laboratory tests and a questionnaire on lifestyle factors were also analysed. In the laboratory part of the project, the concentration or value of the following parameters was determined in all patients: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), glucose, total cholesterol, high and low density lipoproteins, triglycerides, uric acid, creatinine and alanine transaminase (ALT).

Blood pressure was measured in all patients using an oscillometric method. In addition, each patient underwent a 12-lead electrocardiogram (ECG) with assessment of the corrected QT interval using the Bazett formula.

The anatomy and function of the heart were also assessed by echocardiography conducted using a Philips Epiq Elite ultrasonograph. Ultrasound measurements of cIMT were performed using a Toshiba Aplio 400 ultrasonograph. Both the right (RCA) and left (LCA) common carotid arteries were evaluated, and their cIMT values were calculated in percentiles. The obtained results were subjected to statistical analysis.

Continuous variables were presented by median, mean and standard deviation, and qualitative variables by proportions. The conformity of the distribution of continuous variables to a normal distribution was checked using the Kolmogorov-Smirnov test. The statistical significance of the differences between the means of the continuous independent variables with a normal distribution was evaluated using the Student's t-test, and of continuous independent variables with a abnormal distribution using the U-Mann-Whitney test. Categorical variables were compared using the chi2 test with Yates correction for continuity when indicated. Differences were considered statistically significant when the coefficient of statistical significance was below 0.05 (p-value<0.05). Bioethics Committee approval (RNN/101/19/KB) was obtained for the aforementioned studies.

Results

Publication I

The ideal model of cardiovascular health was identified for 22 children (5.6%). The collected data revealed that in terms of the recommended level of physical activity, children from physician families were significantly more likely to meet American Heart Association (AHA) criteria than their peers from other study populations (56.5% vs. 16.6%). There was no correlation between achieving adequate levels of physical activity and body mass index (BMI) ($p > 0.1$). Overweight children had a more balanced diet than children with an appropriate body weight ($p = 0.009$). Discriminant analysis and the Shapiro-Wilk test showed no effect of dietary patterns on physical activity in our study. Based on all the data obtained, it was concluded that despite extensive educational efforts and greater public awareness, children are still exposed to modifiable risk factors for the development of CVD.

Publication II

Four JIA patients had cIMT values above the 94th percentile for age and gender. In addition, a positive correlation between ESR and the RCA dimension (presented as a percentile value) was found. There was also an association between increased cardiovascular risk in JIA patients exposed to second-hand smoking. An abnormal cIMT value was found in 2 of 11 patients whose parents admitted to smoking in the presence of their children, and the difference was statistically significant. Despite the lack of statistical significance, 3 of 4 patients with abnormal cIMT values were found to have HLA B27 antigen. Our study also showed correlations between lower physical activity and time spent in front of screens (phone/tablet/computer/TV). We found that a doubling of daily screen time during the pandemic led to a significant decrease in physical activity among children.

Publication III

CVD risk factors were shown to be prevalent among both JIA patients and the comparison group. In the study group, significantly more children had abnormal BMI ($p=0.006$), while JIA patients had better nutritional status than patients in the comparison group. Children in the study group more regularly consumed fruit ($p=0.021$), and consumed fast foods ($p=0.011$) and sweetened beverages ($p=0.042$) less frequently than children in the comparison group. Dietary habits demonstrated in both the study group and the comparison group were not related to cIMT values, BMI, selected biochemical parameters or perceived pain. In our study, children with worse eating habits (considering both the study group and the comparison group) were found to spend more time in front of a computer screen than children with healthier eating habits (eating fruits or vegetables daily, fish >= 1 time/week, consuming sweetened beverages less than 1 time/week).

Conclusions

Despite the assumption that cIMT measurement may be a potential screening marker of increased cardiovascular risk, the results obtained in the study are insufficient to recommend the use of this test during routine follow-up of children with JIA. JIA patients with active inflammation (including elevated ESR) who are exposed to second-hand smoke may serve as a potential group at higher risk for the development of CVD. JIA patients strive to eat a healthy diet and be as physically active as their healthy peers. Nevertheless, the overall dietary habits of both children with JIA and healthy individuals of the comparison group require improvement. It is worth promoting healthy lifestyles in JIA patients and among healthy children to minimize exposure to CVD risk factors.