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Mean platelet volume in children with attention deficit hyperactivity disorder

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ABSTRACT

The mean platelet volume (MPV), the accurate measure of platelet size, is considered a marker and determinant of platelet function. MPV can be a potentially useful prognostic biomarker in patients with cardiovascular disease. After reviewing literature, we hypothesized that attention deficit hyperactivity disorder (ADHD) in childhood may be a risk factor for coronary heart disease (CHD) in adulthood. The aim of this study was investigation of MPV and platelet count (PLT) in children with ADHD and healthy subjects. The MPV and the PLT were measured in 70 children with ADHD (aged 6–16 years), and compared with 41 healthy controls. The MPV was found to be significantly increased in ADHD group compared to control group ($p = .006$). There was no significant difference in the PLT between groups ($p > .05$). To our knowledge, this was the first study of investigating the levels of MPV and PLT in children with ADHD. Although significance and cause of increased MPV level in ADHD remain unclear in present study, further studies are warranted to investigate relationships among MPV, ADHD in childhood and CHD in adulthood.

Introduction

The typical characteristics of Type A behavior pattern (TABP) includes extremes of competitiveness, aggressiveness, impatience, easily aroused hostility, rapid speech and movements, and time urgency. It was reported that hyperactive boys had higher Type A scores than their comparison peers [1]. Even if it is thought that TABP and hyperactivity have similar configuration correlates [1], TABP and hyperactivity do not differentiated clearly and to some extent they partially overlap in children [2]. Also, TABP and hyperactivity were found to have considerable stability over time [2]. Furthermore, it is considered that TABP is unrelated to physiologic coronary risk factors such as elevated serum cholesterol levels, blood pressure and body mass index (BMI); and appears to be as stable as these risk factors in children and adults [3]. TABP is an indirect risk factor of coronary heart disease (CHD), by attracting potential triggers in early manifestation of cardiac events [4].

It was reported that children with childhood hyperactivity might envisage intima media thickness in adulthood [5]. Subjects with ADHD is associated with elevated BMI compared to controls [6,7]. The risk of cardiovascular events rises with increasing BMI [8]. Although it was unknown the relationship between ADHD in childhood and CHD in adulthood, at least two cases with ADHD using methylphenidate was associated with myocardial infarction, albeit concomitant use of other drugs [9,10]. The relationship between TABP and ADHD, the role of TABP in early manifestation of cardiac events and possibility of intima media thickness in adulthood of hyperactive children may suggest that risk of coronary artery disease may increase in ADHD although there is no published literature about that issue.

The MPV, the accurate measure of platelet size, has been considered a marker and determinant of platelet function. Larger platelets have more granules, aggregate more rapidly with collagen, have higher thromboxane A2 levels and express more glycoprotein Ib and IIb/IIIa receptors than smaller platelets [11]. It was found that larger platelets were hemostatically more reactive than platelets of normal size, increasing the propensity to thrombosis [12]. Accumulating data has shown that elevated MPV is associated with acute myocardial infarction (AMI), and MPV can be a potentially useful prognostic biomarker in patients with cardiovascular disease [13,14]. Also, it is stated that higher MPV is observed in patients with coronary risk factors including hypercholesterolemia, hypertension (HT), obesity, smoking and diabetes mellitus (DM) [13]. These observations suggest a common mechanism by which these risk factors may increase the risk of CHD [13].

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Similarly, elevated MPV may play a role at increased risk of coronary artery disease in people with TABP.

The aim of present study is to investigate MPV and PLT in children with ADHD and healthy subjects. It was hypothesized that children with ADHD have elevated MPV and PLT levels, compared to healthy controls. To our knowledge, this is the first study of investigating the levels of MPV and PLT in children with ADHD.

Methods

Subjects

Seventy drug-free subjects, aged 6–16, who were admitted to GATA Medical Academy and diagnosed as ADHD according to the DSM-IV (*Diagnostic and Statistical Manual of Mental Disorders, 4th edition*) criteria [15] were included in this study. Patients were assessed using parent completed *the Turgay DSM-IV-Based Child and Adolescent Behavior Disorders Screening and Rating Scale* (T-DSM-IV-S) [16]. Forty-one mentally and physically healthy subjects that had similar socio-demographic characteristics were included in the study as a control group. All subjects in the study were outpatients and Caucasians. Subjects who had seizure disorders, mental retardation, autistic disorder, organic brain damage, psychotic disorder, conduct disorder, elevated blood pressure or HT, hypercholesterolemia, any other acute or chronic physical illnesses, a history of any drug use during the last month or smoking were excluded from the study. Written informed consent was obtained from parents of all subjects. Ethic Committee approved this study. Height, weight, platelet count and MPV were measured and recorded for each subject. The reference range for MPV was between 6.9 and 10.8 fL. There was no child who had an elevated MPV for age.

Blood analysis

Blood samples were drawn after a fasting period of 12 h. In fasting venous blood samples collecting with K3EDTA containing sterile Vacutainer tubes, complete blood counts including MPV were determined by using Abbott Sapphire Automated Hematology Analyzer (Abbott Laboratories, Abbott Park, IL, USA) with its own commercial kits. In order to measure MPV more reliable and to minimize the potential influence of anticoagulant (EDTA) on the MPV, blood samples were analyzed within 60 min after venipuncture.

Statistical analysis

Measures of MPV and PLT in the children with ADHD and control subjects were compared by using two-tailed *t*-test. The comparison of sex in groups was performed by using Chi square test. Results were considered significant, when the p value was <.05.

Results

The age range of the ADHD group was between 6 and 16 years (9.9 ± 2.4 years), and that of the normal control group was between 6 and 16 years (9.5 ± 2.7 years). There was no significant difference in age of the children between the two groups ($p > .05$). ADHD group consisted of 21 girls and 49 boys and control group 14 girls and 27 boys. No significant difference was found in the female/male ratio between ADHD group and control group ($p > .05$). The MPV was found to be significantly increased in ADHD group compared to control group (8.35 ± 0.82 vs. 7.90 ± 0.82 fL; $p = .006$) (Table 1). There was no significant difference in PLT and BMI between groups (both p value >.05).

Discussion

The findings of present study indicate that the children with ADHD may have increased levels of MPV in the absence of related factors, such as elevated blood pressure or HT, hypercholesterolemia and obesity. To the best of our knowledge, this is the first study investigating the levels of MPV and PLT in ADHD.

MPV is considered to be an indicator of platelet activation, and to be important in the pathophysiology of CHD [13,17]. CHD is a manifestation of atherosclerosis which is known to begin in childhood. For atherosclerosis, there are behavioral risk factors (such as hyperactivity, anger, hostility, depression, Type A behavior) that may originate in early childhood and traditional risk factors (such as smoking, obesity, dyslipidemia, DM, HT) which may be a link through which early life behavioral risk factors affect later atherosclerosis [5].

In researches, atherosclerosis is widely assessed by non-invasive markers, such as carotid artery intima media thickness (cIMT) [18]. cIMT is significantly higher in pediatric populations with increased cardiovascular risk factors, such as obesity, insulin dependent DM, dyslipidemia and HT, compared with healthy populations [19]. Conversely, no association between cIMT and non-alcoholic fatty liver disease (NAFLD) was found in children and adolescents [20]. These findings confirm early vascular damages in pediatric populations with an increased future risk for CHD [19].

Moreover, relationship between behavioral and traditional risk factors is intriguing. Childhood hyperactivity predicts adulthood cIMT after adjustment for childhood and adulthood risk factors for atherosclerosis in women [5]. Motor activity, even hyperactivity, in childhood was found to increase significantly with the ApoE phenotypes in the order of E2/2, E3/2, E4/2, E3/3 and E4/4 [21]. Total cholesterol levels and ApoE phenotype in childhood correlate with arterial atherosclerotic findings [22]. It was reported that childhood hyperactivity correlated with apolipoproteins A-I and B (with high B and low A-1) [23] and precursors of insulin resistance syndrome [24]. Also, childhood hyperactivity was shown to predict young adulthood obesity [25].

MPV is also thought to be able to reflect atherosclerosis [13]. Previous studies reported controversial results about the relationship between MPV and cIMT. Arslan et al. [26] found that MPV and the left cIMT were significantly higher in obese adolescents than the healthy controls. MPV was found to significantly correlate with cIMT in obese adolescents, independently of fatty liver grade, relative weight, total cholesterol and homeostasis model of assessment of insulin resistance [26]. Similarly, Yarlioglues et al. [27] reported a positive correlation between MPV and cIMT in 80 newly diagnosed adult hypertensive patients. On the contrary, Kilciler et al. [28] reported no relationship between MPV and carotid atherosclerosis in adult patients with NAFLD. While Arslan et al. [26] suggested that MPV might be used as a possible indicator of subclinical atherosclerosis in obese adolescents, Kilciler et al. [28] suggested that MPV might not be involved in the mechanism of increased cardiovascular risk in adults with NAFLD in the absence of other metabolic risk factors such as hypertension, diabetes and obesity.

There are numerous studies investigating the relationship between MPV and risk factors for CHD, including DM [29–32], HT [32–36], hypercholesterolemia [37–39], smoking [40,41], obesity [26,35,42,43] and metabolic syndrome (MetS) [44,45]. Several studies demonstrated that MPV increased in the presence of DM [29–32] and in patients with impaired fasting glucose (although less than that in diabetic subjects) [46,47]. It was showed that no change in MPV between Type 1 and Type 2 diabetes [29]. It is suggested that the increase in MPV may occur due to the diabetic state