Homocysteine levels in Turkish children

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ABSTRACT

Hyperhomocysteinemia is a known risk factor for cerebrovascular, peripheral vascular, coronary heart disease, and thrombosis. Several data related to total homocysteine concentrations for children and adolescents were reported from different populations. But no data are available comparing homocysteine levels analyzing according to age ranges in Turkish children. So, we aimed to achieve a reference range for total homocysteine in Turkish children. Plasma total homocysteine concentrations were measured in 177 healthy children within three groups according to age range (1-6, 7-11, 12-17 y). Mean tHcy concentrations were determined (7.77 ± 4.13 µmol/L). Homocysteine were lowest in younger children and increased with age: 1-6 y (3.87 ± 1.44 µmol/L), 7-11 y (8.70 ± 1.40 µmol/L), and 12-17 y (13.54 ± 1.49 µmol/L). We observed no significant differences in tHcy values between girls and boys in all groups. We suggest that total homocysteine levels must be evaluated in children according to age.

Key Word: Homocysteine, Child.

ÖZET

Türk çocuklarında homosistein düzeyleri

Hiperhomosisteinemi serebrovasküler, periferik vasküler, koroner kalp hastalıkları ve tromboz için bilinen bir risk faktörüdür. Total homosistein düzeyleri ile ilgili olarak farklı topluluklarda çocuk ve erişkinlerden çeşitli bildirimler yapılmıştır. Ancak Türk çocuklarında belirli yaş aralıklarında homosistein düzeylerini karşılaştıran çalışma yoktur. Bu nedenle, biz Türk çocukları için referans aralıklarını belirlemeye çalıştık. Sağlıklı 177 çocuk, yaş aralıklarına göre (1-6, 7-11 ve 12-17) gruplandırıldı ve plazma total homosistein düzeyleri (tHcy) ölçüldü. Ortalama tHcy belirlendi (7.77 ± 4.13 µmol/L). Homosistein genç çocuk ve adölesanlarda düşük iken yaşla artmakta idi. 1-6 y (3.87 ± 1.44 µmol/L), 7-11 y (8.7 ± 1.4 µmol/L) ve 12-17 y (13.54 ± 1.49 µmol/L). Tüm gruplarda erkek ve kız çocuklar arasında fark saptamadık. Bu verilere göre çocuklarda homosistein düzeyleri yaşa göre değerlendirilmelidir.

Anahtar Kelime: Homosistein, Çocuk.

INTRODUCTION

Homocysteine is a sulfur amino acid derived from methionine during transmethylation. It is either salvaged back to methionine in a folate- and cobalamin-dependent remethylation reaction or transformed into cysteine via the vitamin B6 -dependent enzyme cystathionine ß-synthase. Homocysteine levels increase in the deficiency of folic acid and vitamin B12. Further, genetic alterations in the cystathione ß-synthase (CBS) and methylenetetrahydrofolate reductase (MTHFR) genes may account for reduced enzyme activities and elevated plasma homocysteine levels[1-3]. Homocysteinuria refers to a group of rare inborn errors of metabolism resulting in high concentrations of circulating homocysteine and urinary homocysteine. A characteristic feature of this disorder is premature vascular disease. If the homocysteinureia is left untreated, 50% of patients will have thromboembolic events before the age of 30 years[1].

Clinical and epidemiologic studies showed a relation between total plasma homocysteine (tHcy) concentrations and coronary artery disease as well as peripheral artery disease, stroke, and venous thromboembolism[4-10]. Because the prevalence of hyperhomocysteinemia ranges from 20% to 40% in different populations with coronary artery disease, the therapeutic control of elevated homocysteine concentrations may be important in the prevention of premature vascular disease[2].

Age- and sex-specific reference intervals for tHcy concentrations in adults have been established[11,12]. However, data for children and adolescents are few and were from different populations (Norway, Spain, USA, Belgium). Although, recently homocysteine values in epileptic Turkish children were reported, no data are available comparing homocysteine levels analyzing according to age ranges in Turkish children[13]. So we aimed to study the distribution of tHcy in a healthy Turkish pediatric population.

MATERIALS and METHODS

Our study included 177 healthy children examined in the outpatient unit of Pediatrics Department of Ankara University Medical School, (90 female, 87 male, age range 1 to 17). Data on birth date, personal history (e.g., history of chronic disease -renal, heart, respiratory, endocrine, or neurologic disease-); familial history of neural tube defects; familial cardiovascular disease (coronary artery disease, stroke, or peripheral vascular disease in at least one family member), and vitamin supplementation were obtained with a self-administered questionnaire and all positive individuals were excluded. Informed consent was obtained from at least one of the parents. The children were classified in three groups according to their age. After 12 hours fasting, blood specimens with EDTA were drawn from the patients. Plasma homocysteine levels were measured using AxSYM Homocysteine assay (Abbott, Wiesbaden, Germany).

Statistical Analysis

Results were expressed in mean ± SD. For analysis of data, one-way ANOVA and independent T-test were used; $p< 0.05$ was considered as significant.

RESULTS

Mean homocysteine level was 7.77 ± 4.13 Mmol/L. Homocysteine levels for each group were shown in Table 1. Total homocysteine concentrations in each group (1-6, 7-11, 12-17 y) were (3.87 ± 1.44), (8.70 ± 1.40), (13.54 ± 1.49)

Table 1. Homocysteine levels in healthy children

Age (year)	tHcy (Mmol/L)
1-6 (n: 77)	3.87 ± 1.44
7-11 (n: 57)	8.70 ± 1.40
12-17 (n: 43)	13.54 ± 1.49

respectively. None of the children in each age group have homocysteine levels over 15 µmol/L which is considered to be cut off value for the adults. The mean tHcy concentration in each age group was significantly different from that in the other age group and total homocysteine levels increased significantly with age ($p< 0.05$). There weren't significant differences between boys and girls in all groups ($p> 0.05$) (Table 2).

DISCUSSION

Homocysteine is an independent risk factor for atherosclerotic vascular disease unrelated to hyperlipidemia, hypertension, diabetes, and smoking. In adults, the effect of age on basal tHcy concentrations was very well established. With each 5 µmol/L rise in total homocysteine levels, the risk for coronary artery disease was increased by 60% for men and by 80% for women[14]. However, very few studies have investigated tHcy concentrations in children.

Vilaseca et al measured tHcy concentrations in 195 Spanish children and adolescents aged 2 mo to 18 y. The investigators established 3 age groups for whom tHcy concentrations were most significantly different after statistically analyzing all age groups: 2 months to 10 y, 11-15 y, and 16-18 y[15]. In Norway, Tonstad et al studied the relation of tHcy, lipid, and apolipoprotein B concentrations in children with premature cardiovascular disease in family members. In children aged 8-12 y, the mean tHcy concentration was 5.3 µmol/L[16]. Reddy measured tHcy values in children in 4 age groups (15 boys and 15 girls in each group) from the New Orleans area. They observed no significant changes in the age groups or between the sexes[17]. De Laet et al measured tHcy concentrations pre-school children in Belgium. Children were separated to three age groups. Total homocysteine was also significantly increased with age. The median tHcy concentration in the oldest age group was significantly different between girls and boys[18].

Our data is in concordance with the previous reports and revealed once more that total homocysteine levels must be evaluated according to age in children. Evaluating the range of homocysteine levels in children according to age would make protective treatment a current issue for some disorders such as thrombosis and early arteriosclerosis.

Table 2. Age and sex-dependent reference ranges for total homocysteine

			Concentration (Mmol/L)		
Age (years)	**Sex**	**n**	**Mean**	**(SD)**	**p**
1-6	M	34	3.66	1.42	0.24
	F	43	4.04	1.45	
7-11	M	30	8.70	1.32	0.99
	F	27	8.70	1.50	
12-17	M	23	13.58	1.48	0.85
	F	20	13.50	1.54	

Significance of difference of mean between sexes was calculated using independent-samples T-test; a p value of < 0.05 was considered significant.

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