Evaluation of Neurodevelopment Using Bayley-III in Children with Cyanotic or Hemodynamically Impaired Congenital Heart Disease

Olgu Hallioglu, MD,*† Guliz Gurer, MD,* Gulcin Bozlu, MD,* Derya Karpuz, MD,*† Khatuna Makharoblidze, MD,* and Cetin Okuyaz, MD*‡

*Department of Pediatrics, Divisions of †Pediatric Cardiology and ‡Pediatric Neurology, University of Mersin Faculty of Medicine, Mersin, Turkey

ABSTRACT

Objective. The purpose of this study was to compare neurological development of children with cyanotic or hemodynamically impaired congenital heart disease (CHD) and healthy controls by using "Bayley Scales of Infant and Toddler Development Screening Test, Third Edition" (Bayley-III).

Patients. Children with CHD (n = 37) and healthy controls (n = 24) aged between 1 and 41 months who were admitted to the Department of Pediatric Cardiology at our university hospital were included. The participants were assessed using Bayley-III test. All patients had cyanotic or hemodynamically impaired CHD. Weight, height, body mass index (BMI), mid-arm circumference (MAC), triceps skinfold thickness (TSF), and head circumference (HC) were measured and standard deviation scores (SDSs) were determined.

Results. SDS values of weight, height, BMI, MAC, and TSF of the patients as well as HC values were significantly lower than the control group ($P < .001$). Compared with controls, the patients had significantly lower mean scores in all Bayley-III subscales ($P < .001$). We observed similar results in Bayley-III scores including the mean values of cognitive, language, and global motor scores for the CHD patients with and without cardiac surgery ($P > .05$).

Conclusion. This study demonstrated that children with cyanotic or hemodynamically impaired CHD have delayed neurodevelopmental outcomes compared with healthy children as assessed using Bayley-III.

Key Words. Congenital Heart Disease; Neurodevelopment; Bayley-III Test

Introduction

Congenital heart disease (CHD) is one of the most common birth defects and a significant cause of childhood morbidity and mortality. It has been reported to occur in 4 to 12 per 1000 live births.[1,2] Because of the new surgical techniques and advances in cardiopulmonary bypass, cardiac catheterization, intensive care, noninvasive imaging, and medical treatments, the survival rates of children with CHD have been increasing.[3] With improved surgical outcomes and survival rates, pediatric patients with CHD appear to be at higher risk for neurodevelopmental deficits characterized by mild cognitive dysfunction, social interaction problem, and difficulties in core communication abilities.[4]

"Bayley Scales of Infant and Toddler Development Screening Test, Third Edition" (Bayley-III) is one of the most reliable and widely used tests for growth retardation in children aged 1–42 months. This test was first described in 1969 by Bayley. It was revised in 1993, and recently it was standardized in 2006.[5–7] Cognitive, language, and global motor developments of infants and children are evaluated by Bayley-III test. Language scale is interpreted by two subscores: expressive and receptive communications; the motor development is also evaluated by two subscales: fine and gross motor scores.

This study aimed to compare neurological development of children with cyanotic or hemodynamically impaired CHD and healthy controls by using Bayley-III test.

Methods

Thirty-seven children with CHD between 1 and 41 months of age who followed up at Pediatric Cardiology Outpatient Clinic of Mersin University and 24 healthy controls of the same age group were included in this prospective study. Age- and gender-matched control group consisted of children who were followed up in the well-child clinic. All patients had cyanotic or hemodynamically impaired CHD. Impaired hemodynamic status was defined for children who need medical treatment, surgical operation, or invasive intervention. Children with a history of hypoxic birth, prematurity, hypoglycemia, epilepsy, a neurological disease, or a genetic syndrome were excluded from the study. The study was approved by the local ethics committee (MEU 2011/27).

Body weight, height, mid-arm circumference (MAC), and head circumference (HC) were measured by standard anthropometric techniques and left arm triceps skinfold thickness (TSF) measurements were made with standard Lange calipers by the same staff member. Standardized measures for Turkish children were used for weight, height, and body mass index (BMI, kg/m^2), and standard deviation scores (SDSs) were calculated for each measurement.[8]

Cognitive, language, and global motor developments were evaluated by Bayley-III test, as previously described.[9] Briefly, the cognitive scale includes information processing, information processing speed, problem solving, play skills, and number concepts. The language scale includes both receptive (ability to hear, understand, and respond) and expressive (ability to communicate) communication skills. The motor subtests include quality of movement, sensory and perceptual motor integration, and basic locomotion milestones. The Bayley-III composite test scores are scaled on a range of 40–160, to have a mean of 100, and a standard deviation (SD) of 15. Although not considered an intelligence quotient test, the Bayley Scales reliably identify infants with developmental delays, as indicated by scores less than 85 on the cognitive, language, or global motor composite scores.[7] Tests were performed by one individual (K.M.) who is experienced in testing child development and is blinded to the diagnosis.

Statistical Analysis

The minimum sample size was calculated using Bayley subscale means and SDs of a previous study[10] and obtained as 31 in each group. The power value was .90 and significance value was .05 for this calculation. However, we have reached 37 patients and 24 controls providing inclusion criteria during the study and supplied total sample size that was planned with a priori power analysis. Mean and SD values were given as descriptive statistics. Differences between continuous measurement groups were tested by Student's *t*-test and Mann–Whitney U tests. Bivariate relationships between categorical variables were examined using Pearson's chi-square test. The results were considered statistically significant if *P* values were less than .05.

Results

A total of 61 cases were enrolled in the study. Demographic data of the patients and controls were shown in Table 1. The mean age of patients and controls was 15.7 ± 9.02 and 18.62 ± 10.67 months, respectively ($P = .255$). According to the age range breakdown including <6 months, 6–12 months, 12–24 months, and 24–41 months, the numbers of the patients and the control groups were 3 (8.1%), 14 (37.8%), 14 (37.8%), and 6 (16.2); and 2 (8.3%), 6 (25%), 6 (25%), and 10 (41.7%), respectively, and the groups were not different ($P = .168$). There was no significant difference in gender, age, birth weight, and mother's age between patient and control groups (Table 1). Anthropometric data of the study were presented in Table 2. SDS values of weight, height, BMI, MAC, and TSF of the patients as well as HC values were significantly lower than the control

Table 1. Characteristics of Patients and Controls

	Patient (n = 37)	Control (n = 24)	*P*
Gender			
Female (%)	20 (54.1)	11 (45.8)	.465
Male (%)	17 (45.9)	13 (54.2)	
Age (month)	15.7 ± 9.02	18.62 ± 10.67	.255
Birth weight (g)	2966.62 ± 416.05	3380 ± 514.58	.082
Mother's age (years)	31.26 ± 5.02	30.85 ± 6.45	.791

Table 2. Anthropometric Measurements of Patients and Controls

	Patient (n = 37)	Control (n = 24)	*P*
Weight (SDS)	–1.01 ± 1.34	0.45 ± 0.89	.0001
Height (SDS)	–0.61 ± 1.47	0.66 ± 0.48	.0001
BMI (SDS)	–0.55 ± 1.19	0.65 ± 0.92	.0001
MAC (SDS)	–2.25 ± 1.68	0.81 ± 0.78	.008
HC (cm)	41.72 ± 3.49	44.95 ± 2.74	.004
TSF (SDS)	–9.25 ± 1.65	–7.96 ± 1.81	.003

BMI, body mass index; HC, head circumference; MAC, mid-arm circumference; SDS, standard deviation score; TSF, triceps skinfold thickness.

group. The diagnosis of the patients with CHD was shown in Table 3. Mean values of cognitive, language, and global motor scores in addition to their subscores, namely receptive communication, expressive communication, fine motor, and gross motor scores, were shown in Table 4. Compared with controls, the patients had significantly lower mean scores in all Bayley-III subscales. Similar results in Bayley-III scores were observed including the mean values of cognitive, language, and global motor scores for the CHD patients with (n = 16) and without (n = 21) cardiac surgery (87.64 ± 15.02 vs. 86.04 ± 20.11, $P = .802$; 91.21 ± 11.79 vs. 81.23 ± 15.34, $P = .226$; 92.33 ± 13.99 vs. 83.80 ± 13.01, $P = .135$, respectively). There was no significant difference in Bayley-III scores between the patients with cardiac surgery before and after 12 months of age.

Discussion

In this study, we have found lower scores in all Bayley-III subscales in children with CHD, which has directly measured normal control group from the same population of patients. The vast majority of reports of neurodevelopmental outcome in CHD do not have a direct control group but rely on the standardized reference population for the test.

With improvement of the survival rate due to advances in pediatric cardiology, pediatric intensive care, and new techniques of cardiovascular surgery, survivors among children with CHD are at risk for neurodevelopmental morbidity.[4] Neurodevelopmental status of children with CHD is affected by several environmental and biological factors. For predicting worse neurodevelopmental outcome, assessment of these factors in children with CHD is important. However, we found that there were statistically significant differences between patient and control groups for anthropometric measurements including weight, height, BMI, MAC, HC, and TSF. As in our study, growth restriction remains an ongoing problem in infants and young children with CHD.[11] Besides, children with CHD have been found to have greater risk for neurodevelopmental and behavioral problems characterized by mild cognitive impairment, attention problems, impaired social interaction, fine and gross motor delays, deficits in visual construction and perception, impairments in core communication skills, including pragmatic language, as well as inattention, impulsive behavior, and impaired executive function.[12] Although test-related problems have been described,[13] it has been reported that the current reference standard is Bayley-III for evaluating neurodevelopmental status.[14] In the present study, neurodevelopmental outcome was assessed with Bayley-III, which evaluates five different scales including cognitive; language scale, consisting of receptive and expressive communication subtests; and motor, consisting of fine and gross motor subtests. Thus, our study demonstrated that statistically significant retardation has been detected in all subscales of Bayley-III in children with CHD rather than the controls.

Several studies have investigated the neurodevelopmental outcomes of cardiac surgery in children with CHD. Besides the impact of chronic hypoxemia caused by underlying CHD, 30–50% of infants who underwent surgery in the neonatal period have a pattern of neurodevelopmental problems with general intelligence, receptive and

Table 3. Diagnosis of the Patients

Diagnosis	n (%)
VSD	12 (32.4)
Tetralogy of Fallot	7 (18.9)
Large ASD	4 (10.8)
Transposition of the great arteries	4 (10.8)
AVSD	3 (8.1)
DORV	2 (5.4)
Pulmonary atresia	2 (5.4)
Complex cyanotic heart disease	2 (5.4)
Aortic stenosis	1 (2.7)

ASD, atrial septal defect; AVSD, atrioventricular septal defect; DORV, double outlet right ventricle; VSD, ventricular septal defect.

Table 4. Mean Scores of Bayley-III in Patients and Controls

	Patient (n = 37)	Control (n = 24)	*P*
Cognitive	87.36 ± 16.79	101.18 ± 11.88	<.0001
Language	87.63 ± 14.15	104.95 ± 13.65	<.0001
Receptive communication	8.71 ± 2.74	12.04 ± 2.66	.003
Expressive communication	6.92 ± 2.25	9.68 ± 2.54	.009
Global motor	86.66 ± 17.95	102.92 ± 12.54	<.0001
Gross motor	6.96 ± 3.54	9.68 ± 2.62	.005
Fine motor	8.58 ± 3.46	11.45 ± 2.12	<.0001

Bayley-III, Bayley Scales of Infant and Toddler Development Screening Test, Third Edition.

expressive language, and gross and fine motor functioning.[15] We observed similar results in Bayley-III scores for the CHD patients with and without cardiac surgery. We also found that the patients who underwent cardiac surgery before and after 1 year old had similar mean scores of Bayley-III. However, Walker et al. evaluated the developmental outcomes following major noncardiac and cardiac surgery in term infants.[10] They found that the infants who underwent major noncardiac and cardiac surgery had significantly lower mean scores of Bayley-III. In a retrospective cohort study, Andropoulos et al. reported an association between perioperative anesthetic exposure and neurodevelopmental outcome scores using Bayley-III at the age of 12 months in neonates who underwent complex cardiac surgery.[16] On the other hand, Guerra et al. found no association between exposure to any class of anesthetic or sedative agent and significant neurodevelopmental delay in a prospective follow-up project.[17]

The most obvious limitation of our study was the small number of patients. On the other hand, the strength of the study is the use of normal control group from the same patient population. Further studies are required to evaluate a large number of cases. It has been demonstrated that implementation of a routine developmental follow-up program for CHD patients is possible and useful in identifying those patients who would benefit most from early intervention.[18] In our study, in spite of the limited patients, we have concluded that children with cyanotic or hemodynamically impaired CHD have delayed neurodevelopmental outcomes compared with healthy children as assessed using Bayley-III.

In order to assist optimal social and academic adjustment of CHD patients, detailed growth parameters and screening with developmental testing could be considered during long-term follow-up.

Authors' Contributions

Olgu Hallioglu conceptualized and designed the study, drafted the initial manuscript, and approved the final manuscript as submitted.

Guliz Gurer and Gulcin Bozlu were involved in the concept and design of this project, interpretation of the data, and the manuscript preparation.

Derya Karpuz and Khatuna Makharoblidze carried out the initial analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Cetin Okuyaz provided consultation throughout all stages of the project including planning, implementation, and manuscript preparation.

Corresponding Author: Olgu Hallioglu, MD, Department of Pediatrics, Division of Pediatric Cardiology, University of Mersin Faculty of Medicine 34. Cadde, Ciftlikkoy Kampusu, Mersin 33343, Turkey. Tel: +90-324-241-0000; Fax: +90-324-241-0000; E-mail: olguhallioglu@yahoo.com

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