RESEARCH ARTICLE

POST-OPERATIVE NEURODEVELOPMENTAL FINDINGS IN SYNDROMIC AND NON-SYNDROMIC CRANIOSYNOSTOSIS

ABBAS NEJAD Enayatollah MD[1]
NIKOOBAKHAT Mehdi MD[2]

1. Professor of Neurosurgery, Iran University of Medical Sciences, Tehran, Iran
2. Resident of Neurosurgery, Iran University of Medical Sciences, Tehran, Iran

Corresponding Author:
NIKOOBAKHAT Mehdi MD
Firoozgar Hospital, Tehran, Iran
Tel: +98 2182141393,
E-mail: mnikobakht@gmail.com

Received: 12-Oct- 2009
Last Revised: 20-Feb- 2010
Accepted: 22-Feb- 2010

Abstract

Objective

To evaluate the developmental situation of children that undergo operation because of syndromic and non-syndromic craniosynostosis.

Materials & Methods

In this prospective study, 24 children (4 to 16 months of age) who underwent neurosurgeryical intervention because of non-syndromic (79%) and syndromic (21%) craniosynostosis were recruited. For psychological evaluation, the Bayley Scales of Infant Development-Second Edition (BSID-II) was applied one month before and one year after surgical correction. The scale consists of three parts, Mental Developmental Index (MDI), Psychomotor Developmental Index (PDI), and Behavior Rating Scale. The MDI and PDI yield age-standard scores (100 ± SD).

Results

Mean baseline BSID-II scores revealed a mild delay in mental and motor scores (MDI: 84.3±2.1; PDI: 80.5±4.2) in non-syndromic craniosynostosis and a moderate delay in mental and motor scores (MDI: 70.3±3.1; PDI: 64.3±1.7) in syndromic craniosynostosis. Mean postoperative BSID-II score revealed improved motor scores (MDI: 91.3±0.1; PDI: 91.3±0.2) in non-syndromic craniosynostosis and mean postoperative BSID-II score revealed a mild delay in mental scores and no change in PDI. Among children with syndromic craniosynostosis, mean BSID-II score indicated mild baseline deficits in both mental and motor scores post operatively.

Conclusion

Mental development and prognosis was better in non-syndromic craniosynostosis comparing syndromic craniosynostosis. Surgery is effective in neurodevelopmental growth in non syndromic types of craniosynostosis but in syndromic type, remodeling surgery does not significantly affect neurodevelopmental outcome.

Keywords: Craniosynostosis, BSID-II, Neurodevelopmental

Introduction

The osseous cranial base is embryologically derived from a cartilaginous framework (endochondral bone), which undergoes a proliferative growth pattern. In contrast, the calvarium consists of membranous bone, which has no cartilaginous phase. The calvarium grows by depositing new bone along suture

lines in response to the distending forces of the rapidly growing brain. During the first two years after birth, the brain increases in size to 75 percent of its adult volume (1).

Craniosynostosis is the premature and abnormal fusion of one of the six suture lines that form the living skull. This abnormal fusion results in an abnormal head shape from aberrant bone growth patterns and, if uncorrected, can lead to increased intracranial pressure (ICP) and abnormalities in the shape and symmetry of the craniofacial skeleton.

Premature closure of any of the calvarial sutures prevents separation of the calvarial bones and produces a restriction on growth vectors leading to a morphologic change in calvarial shape (2).

Passage of the head through the birth canal deforms the head. This shape is retained for 2-3 weeks postnatally, making the diagnosis of craniosynostosis by a pediatrician difficult in the neonatal period. Therefore, most cases are detected in the perinatal period and occasionally during later infancy. Diagnosing craniosynostosis early in the perinatal period is important because the brain grows rapidly during this period and a delay only worsens the deformity of the head shape. The clinical diagnosis is not difficult because each suture fusion is characterized by a specific calvarial deformity (3).

There are numerous types of craniosynostosis. In general, craniosynostosis is divided as syndromic and nonsyndromic, and different names are given to the various types of non syndromic craniosynostosis depending on which suture, or sutures, are involved (3).

The purpose of neurodevelopmental testing is to obtain information about the cortical functioning prior to and after cranial vault remodeling. The Bayley Scales of Infant Development–II (BSID-II) is commonly used to procure this information. These tests compare the child's mental and psychomotor scales with a normogram and thus help in quantifying whether the child is delayed and whether the surgery will help to reduce the severity of the delay (4).

The greatest difficulty with neurodevelopmental testing is the lack of accuracy in measuring cortical function in an infant at 3-6 months of age. At risk children who show delays at 12 months do correlate with scores of development at 4.5 years of age. Similarly, at-risk children assessed at 6 months have scores predictive of intelligence scores at 24 and 48 months. Understandably, an infant aged 3 months cannot be tested for language delays, but the BSID-II is a comprehensive test of various aspects of an infant's developmental skills and does not produce isolated findings. These factors make BSID-II the most reliable assessment tool for infants (4, 5,6,7).

Timing of surgery and optimization of the growth potential of the brain in the early perinatal period are controversial issues in surgical management of both types of craniosynostosis. In review of literature, documented data is not sufficient for a definite protocol for neurosurgeons. Therefore, we decided to study this important challenge that exists among neurosurgeons and neurologist. Furthermore, complications in early surgery, confines decision making for neurosurgeons regarding the best chance for having a good functional child in the future.

Materials & Methods

Children that were operated because of craniosynostosis in Firoozgar Hospital entered this study. Twenty-four patients were evaluated pre-operatively and 17 of them were also evaluated post-operatively. Patients were divided into non-syndromic and syndromic craniosynostosis.

Psychological evaluation was achieved using the Bayley Scales of Infant Development-Second Edition (BSID-II) within 2 months before and again one year after surgical correction. The BSID-II is a widely used measure of infant cognitive and motor development. The scale consists of three parts, Mental Developmental Index (MDI), Psychomotor Developmental Index (PDI), and Behavior Rating Scale.

For statistical analyses, mean values of BSID-II subscales were reported. The Mann-Whitney U test was used for comparison of MDI and PDI before and after surgery between non-syndromic and syndromic groups. To determine the significance level of PDI and MDI changes after surgery in each group, the Wilcoxon signed ranks test was used.

We performed data analyses focusing on specific aspects of the test score distributions. First, we compared the proportion of patients and controls testing in the "delayed" range (that is, scores , 85 for the MDI or PDI) at the first and second visits by fitting logistic regression models.11 The logistic regression model is used to compare the odds of developmental delay in patients with that in controls. Second, we compared the proportions of patients and controls in categories corresponding to more severe developmental delay (categories being from a four-category ordered categorical grouping of test scores: accelerated; 115,within normal limits; 85–115, mildly delayed; 70–84; moderate or severely delayed;70) by fitting ordered logistic regression models (8).

Results

The children ranged in age from 4 to 16 months at the time of the craniofacial reconstruction (mean age: 8.9 months). Non-syndromic craniosynostosis was diagnosed in 79 percent and syndromic craniosynostosis in 21 percent of the patients. Mean baseline BSID-II scores revealed a mild delay in mental and motor scores (MDI: 84.3±2.1; PDI: 80.5±4.2) in non-syndromic craniosynostosis and a moderate delay in mental and motor scores (MDI: 70.3±3.1; PDI: 64.3±1.7) in syndromic craniosynostosis. Significant differences were observed between non-syndromic and syndromic MDI and PDI mean values before surgery ($P < 0.001$).

In Table 1, mean values of MDI and PDI scores in the two studied groups before and after surgery are presented. As shown, a significant change was observed in MDI and PDI in the non-syndromic group. However, such a difference was not observed in the syndromic group.

The differences in the mean values of MDI and PDI following surgery between non-syndromic and syndromic groups were statistically significant ($P <0.001$) (Table 2).

Table 1. Comparison of pre- and post-operation mean values of BSID-II in patients with non-syndromic and syndromic craniosynostosis.

	BSID-II	Pre-operation	Post-operation	P value
Non-syndromic	MDI	84.3±2.1	91.3±0.1	< 0.001
	PDI	80.5±4.2	91.3±0.2	< 0.001
Syndromic	MDI	70.3±3.1	70.1±1.2	0.317
	PDI	64.3±1.7	65±0.8	0.180

Table 2. Comparison of patients with non-syndromic and syndromic craniosynostosis of pre- and post-operation mean values of BSID-II.

	BSID-II	Non Syndromic	Syndromic	P value
Pre operation	MDI	84.3±2.1	70.3±3.1	< 0.001
	PDI	80.5±4.2	64.3±1.7	< 0.001
Post operation	MDI	91.3±0.1	70.1±1.2	< 0.001
	PDI	91.3±0.2	65±0.8	< 0.001

Discussion

Craniosynostosis or the premature fusion of calvarial sutures may involve a single or multiple sutures. Multiple-suture craniosynostosis is commonly associated with abnormalities of other organ systems and manifests with varying degrees of developmental delays (9).

Children with syndromic craniosynostosis characterized by multisystem involvement are often delayed. This delay can be severe and the child may be classified as mentally retarded. However, children with single-suture craniosynostosis do not commonly have significant delays (10).

Multiple theories have been proposed for the etiology of primary craniosynostosis, but the most widely accepted is a primary defect in the mesenchymal layer ossification in the cranial bones and The syndromic causes appear to result from genetic mutations responsible for fibroblast growth factor receptors 2 and 3. A gene locus for single suture craniosynostosis has not been identified (11).

Virchow initially proposed that the cranial suture in cases of craniosynostosis was abnormal and therefore responsible for premature closure (12, 13). A recent study by Eaton et al showed that primary alteration of the calvarial shape would cause a secondary deformation of the cranial base but not vice versa (14). Kapp-Simon et al. reported that the mean score of the subjects with craniosynostosis was 103 (SD: 15.8), which was not different from that of the typical population (15).

However, the BSID does not differentiate between mental and motor functioning, as does the BSID-II. Speltz et al. compared mental and psychomotor development of infants with non-syndromic sagittal synostosis and compared them with demographically and age-matched subjects without congenital defects (16). A repeated measures multivariate analysis of variance test revealed no statistically significant differences between the frequency of mental retardation within the two groups. However, the study did not specifically compare the incidence of minor developmental delays between the two groups. This issue was addressed by Kapp-Simon in a presentation in which she detected a trend toward an increased incidence of learning disorders, which were often characterized by deficits of executive functions in children with nonsyndromic craniosynostosis. In her later study on global intellectual development and learning disorders of children with nonsyndromic craniosynostosis, she did not detect a variation in the normal distribution. However, she did document an increased incidence of mental retardation in children with nonsyndromic craniosynostosis that was two to three times more than the expected frequency, on the basis of normative data (15). Similarly, two other

studies documented an increased incidence of minor learning disorders in children with isolated sagittal synostosis and isolated metopic synostosis (17,18). Kapp-Simonalso documented an increased frequency of learning disorders in similar subjects (15). This raises the issue of whether the detection of minor mental and psychomotor delays is more pertinent for these subjects rather than the detection of severe developmental delays (i.e., mental retardation). The extent of cortical impairment may not be severe enough to result in global severe developmental delays resulting in mental retardation but may be focal and result only in minor developmental delays and minor learning disorders Our study sought to evaluate the prevalence of developmental delays in two different groups of children with cranial anomalies (i.e. syndromic and non syndromic craniosynostosis) before and after reconstructive operation. In this study we found developmental delays, particularly in the area of motor development which correlates with published findings in older children who demonstrate minor learning disorders.

The role of surgery in neurodevelopmental outcome and reconstructive correction of premature closure of skull sutures is one of the most challenging concerns among neurosurgeons. Comparison of this article with related articles indicates that neurosurgery improves the outcome of the patients with craniosynostosis.

Review of the literature did not yield any practical guides regarding the efficacy of surgery in neurodevelopmental outcome in craniosynostosis, so the authors tried to depict this view of management in this study. Because of the small number of the cases and due to the lack of comparative data (i.e. case and control group), studies with larger sample sizes are recommended.

In conclusion, in patients with non syndromic craniosynostosis, BSID-II scores revealed a mild neurodevelopmental delay preoperatively that improved after remodeling surgery with difference being significant in psychomotor scores. A moderate to severe neurodevelopmental delay was seen in syndromic craniosynostosis, such as crouzon syndrome, that was accompanied by no considerable changes in mental and psychomotor scores after surgical procedures. Neurodevelopment and prognosis was better in non syndromic craniosynostosis than syndromic craniosynostosis. Children with syndromic forms of craniosynostosis (e.g. crouzon syndrome) can be affected by variable degrees of developmental delay which becomes apparent later on in life. Surgery is effective in neurodevelopmental growth in non syndromic types of craniosynostosis but in the syndromic type, remodeling surgery does not significantly affect the neurodevelopmental outcome.

References

1. Kapp-Simon KA. Mental development and learning disorders in children with single suture craniosynostosis. Cleft Palate Craniofac J 1998;35:197-203.
2. Arnaud E, Renier D, Marchac D. Prognosis for mental function in scaphocephaly. J Neurosurg 1995;83:476-79.
3. Mulliken JB, Vander Woude DL, Hansen M, LaBrie RA, Scott RM. Analysis of posterior plagiocephaly: deformational versus synostotic. Plast Reconstr Surg 1999;103:371-80.
4. Bayley N. The Bayley Scales of Infant Development. 2nd ed. The Psychological Corporation: San Antonio, Texas;1993.
5. Connolly BH, Dalton L, Smith JB, Lamberth NG, McCay B, Murphy W. Concurrent validity of the Bayley Scales of Infant Development II (BSID-II) Motor Scale and the Peabody Developmental Motor Scale II (PDMS-2) in 12-month-old infants. Pediatr Phys Ther 2006;18:190-96.
6. Provost B, Heimerl S, McClain C, Kim NH, Lopez BR, Kodituwakku P. Concurrent validity of the Bayley Scales of Infant Development II Motor Scale and the Peabody Developmental Motor Scales-2 in children with developmental delays. Pediatr Phys Ther 2004 Fall;16(3):149-56.
7. Liao HF, Yao G, Wang TM. Concurrent validity in Taiwan of the Comprehensive Developmental Inventory for Infants and Toddlers who were full-term infants. Percept Mot Skills 2008Aug;107(1):29-44.
8. Hosmer DW Jr, Lemeshow S.Applied Logistic Regression. Wiley: New York;1989.

9. Crowe TK, Deitz JC, Bennett FC. The relationship between the Bayley Scales of Infant Development and preschool gross motor and cognitive performance. Am J Occup Ther 1987;41:374-78.
10. Farran DC, Harber LA. Responses to a learning task at 6 months and I.Q. test performance during the preschool years. Int J Behav Dev 1989;12:101-114.
11. Robin NH. Molecular genetic advances in understanding craniosynostosis. Plast Reconstr Surg Mar 1999;103(3):1060-70.
12. Virchow R. Uber dem Cretinismus, namentlich in Franken und uber pathologische Schadelformen. Verhd. Physik. Med Gesell Wurzburg 1851; 2: 230-270.
13. Moss ML,Young RW. A functional approach to craniology. Am J Phys Anthropol 1960;18:281-92.
14. Eaton AC, Marsh JL, and Cheverud JM. The effect of artificial calvarial modification on endocranial base morphology. Plastic Surgery Educational Foundation Scholarship Essay 1997.
15. Kapp-Simon, K A. Psychological and developmental consequences of craniosynostosis. Presented at the Annual Meeting of the American Cleft Palate-Craniofacial Association: San Diego, Calif.April 1996.
16. Speltz ML, Kapp-Simon K,Cunningham M, Marsh J, Dawson G. Single-Suture Craniosynostosis: A Review of Neurobehavioral Research and Theory. Journal of Pediatric Psychology 2004 29(8):651-668.
17. Sidoti EJ Jr, Marsh JL, Marty-Grames L, Noetzel MJ. Long-term studies of metopic synostosis: Frequency of cognitive impairment and behavioral disturbances. Plast Reconstr Surg 1996; 97: 276-81.
18. Rozzelle A, Marty-Grames L, Marsh JL. Speechlanguage disorders in non-syndromic sagittal synostosis. Presented at the Annual Meeting of the American Cleft Palate-Craniofacial Association: Tampa, Fla. April 1995.