

HYPOTONIA IN INFANTS AND YOUNG CHILDREN: AN ETIOLOGICAL ANALYSIS

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ABSTRACT

Objective: To determine the relative frequency of specific disorders that present with hypotonia in Iran.

Methodology: It is a retrospective, cross-sectional study in which 107 children with hypotonia, aged one month to three years, were evaluated in Baqiyatallah Hospital between June 2003 and June 2006. Children were categorized into groups of central and peripheral hypotonia, and specific diagnosis of each of the two groups was made by clinical findings, neuro imaging, metabolic and genetic tests, muscular enzymes, EMG-NCV (Electromyography-Nerve conduction velocity) and thyroid function tests.

Results: Of the 107 infants, one hundred one (94.4%) children had central hypotonia, four (3.7%) had peripheral hypotonia and in two (1.9%) the hypotonia had other causes. The most common cause of central hypotonia was idiopathic central hypotonia thirty four (31.8%), followed by cerebral palsy in twenty two (20.6%), brain structural abnormality in nineteen (17.8%), inborn errors of metabolism fourteen (13.1%), genetic disorders seven (6.5%) and the TORCH (Toxoplasma, Rubella, Cytomegalovirus, Herpes simplex) syndrome three (2.9%).

Conclusion: In our study "central hypotonia" was most prevalent etiology of hypotonia. The most common cause of central hypotonia was idiopathic central hypotonia followed by cerebral palsy, brain structural abnormality, inborn errors of metabolism, genetic disorders and the TORCH syndrome.

KEYWORDS: Hypotonia, Central hypotonia, Peripheral hypotonia.

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INTRODUCTION

Hypotonia is a decreased resistance to passive movement. Hyperextensibility, an

abnormally increased range of joint movement, usually accompanies hypotonia.¹ The central and peripheral nervous system modify tone but intrinsic physical characteristics of tendons, joints and muscles also contribute significantly to tone.² There is an extensive list of conditions associated with the diagnosis of hypotonia, including hundreds of rare diseases.³ Several longitudinal studies support the opinion that majority of hypotonic infants are floppy because of central nervous system dysfunction; some hypotonic infants have genetic disorders and metabolic disturbances, whereas the

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minority of hypotonic infants have neuromuscular and connective tissue disease.^{4,7}

However controversy exists over which of the causes, play a greater role in the frequency of hypotonia.^{2,8} Literature available today shows an extensive list for disorders which may present with hypotonia, and the diagnostic profiles are often complex. As knowledge of the relative frequency of particular disorders that present with hypotonia might help in delineation of appropriate investigations, prevention and treatment, our aim was to gain an insight into the causes of hypotonia in Iran.

METHODOLOGY

A cross-sectional study was performed in the Baqiyatallah Hospital, a tertiary care center and educational hospital, through a search of outpatient records. Children aged between one month and three years, whose predominant problem was hypotonia and had been referred between June 2003 and June 2006 to the pediatric neurology clinic of Baqiyatallah Hospital were enrolled in the study. Hypotonia has been clinically confirmed by the attending pediatric neurologist. Criteria used by the pediatric neurologist to define hypotonia were that the hypotonic child looked floppy, felt floppy, or had hyperextensible joints. Hypotonia is classified as central or peripheral according to the clinical findings (quality of antigravity limb movements, deep tendon reflexes, the child's psychosocial responses) and the result of investigations. If the patients had normal or increased DTR (deep tendon reflexes) and other clinical signs of central nervous system involvement like seizures and mental retardation, they were included in the central group and cranioimaging (CT scan or MRI) was carried out, whereas if they had abnormal facies or dysmorphism, genetic tests were done. Muscle enzymes and EMG-NCV (Electromyography-Nerve conduction velocity) were done for the remaining patients with hypoactive or absent DTR in order to confirm peripheral hypotonia. Thyroid function tests

and metabolic work up were done for all patients.

Eventually 138 infants were included, with 31 of these being excluded from the final analysis because of insufficient information. We also obtained demographic data, prenatal and perinatal factors, physical examination findings (DTR) and paraclinic findings (neuroimaging, EMG-NCV, genetic and metabolic tests, muscular enzymes, thyroid function tests) from the clinical charts. To analyze the findings, we used SPSS software (version 11.5).

RESULTS

Forty nine (45.8%) infants were male and fifty eight (54.2%) were female the mean age of infants was 18.2 ± 9.76 months. Of 107 infants, one hundred one (94.4%) had central hypotonia, four (3.7%) had peripheral hypotonia and two (1.9%) had other causes of hypotonia. The relative frequencies of etiologies are presented in Table-I.

In central hypotonia, the most common causes were idiopathic central hypotonia (31.8%) followed by cerebral palsy (20.6%) and brain structural anomaly (17.8%) respectively. In the central hypotonia group thirty one (30.2%) cases had been delivered by normal vaginal delivery (NVD) and seventy (69.3%) cases by cesarean section. Among children twenty four (23.8%) had a positive history of

Table-I: The relative frequency of etiologies of hypotonia in infants and young children (n=107)

| <i>Etiology</i> | <i>Frequency (%)</i> |
|-----------------------------|----------------------|
| <i>Central hypotonia</i> | 101(94.4) |
| Cerebral palsy | 22(20.6) |
| Brain structural anomaly | 19(17.8) |
| Metabolic disorder | 14(13.1) |
| Genetic disease | 7(6.5) |
| TORCH syndrome | 3(2.9) |
| Stroke | 2(1.9) |
| Idiopathic | 34(31.8) |
| <i>Peripheral hypotonia</i> | 4(3.7) |
| Muscular disease | 2(1.9) |
| Peripheral neuropathy | 2(1.9) |
| <i>Other causes</i> | 2(1.9) |
| Hypothyroidism | 1(0.9) |
| Rickets | 1(0.9) |

Table-II: Results of clinical and paraclinical findings in the three etiologic groups of infants and children with hypotonia (n=107)

| <i>Clinical / paraclinical tests</i> | <i>Result</i> | <i>Central Hypotonia</i> | <i>Peripheral Hypotonia</i> | <i>Other causes</i> |
|--------------------------------------|---------------|--------------------------|-----------------------------|---------------------|
| Deep tendon Reflexes(DTR) | Normal | n=70 (69.3%) | n=1 (25%) | n=2(100%) |
| | Decreased | n=3 (3%) | n=3 (75%) | n=0(0%) |
| Cranioneuroimaging | Increased | n=28 (27.7%) | n=0 (0%) | n=0(0%) |
| | Normal | n=28 (29.4%) | n=3 (75%) | n=2(100%) |
| | Abnormal | n=43 (45.4 %) | n=0 (0%) | n=0(0%) |
| Thyroid function tests | Atrophy | n=24 (25.2%) | n=1 (25%) | n=0(0%) |
| | Normal | n=100 (99%) | n=4 (100%) | n=1(50%) |
| | Abnormal | n=1 (1%) | n=0 (0%) | n=1(50%) |
| Muscular enzymes | Normal | n=13 (76.4%) | n=2 (50%) | n=1(100%) |
| | Abnormal | n=4 (23.5%) | n=2 (50%) | n=0(0%) |
| Metabolic tests | Normal | n=87 (86.2%) | n=4 (100%) | n=2(100%) |
| | Abnormal | n=14 (13.8%) | n=0 (0%) | n=0(0%) |
| Genetic tests | Normal | n=20(74%) | n=2(100%) | n=1(100%) |
| | Abnormal | n=7(26%) | n=0(0%) | n=0(0%) |
| EMG-NCV | Normal | n=10 (100%) | n=1 (25%) | n=0(0%) |
| | Abnormal | n=0 (0%) | n=3 (75%) | n=0(0%) |

birth asphyxia, all of them being from the central hypotonia group. Neither of the two remaining groups had a history of birth asphyxia. There were fifty three (52.5%) cases with neonatal jaundice in the central hypotonia group and three (75%) in the peripheral hypotonia group. There was no history of neonatal hospitalization due to causes other than jaundice in the peripheral hypotonia group, while there were 48 (47.5%) cases with such histories in the central hypotonia group. List of clinical and paraclinical findings in the three groups are summarized in Table-II.

DISCUSSION

Results of this study showed central hypotonia in 101 patients (94.4%) and peripheral in four patients (3.7%). In the Paro-Panjan D et al, study, they found that 88% of cases had central causes of hypotonia, 9% had peripheral causes and 3% remained undiagnosed.⁹The study conducted by Eng GD that included children aged under three years, similar to our study, in this aspect reported that 85% of cases had central causes and 15% had peripheral causes of muscle tone disturbance.¹⁰ Richer et al studied a group of neonate admitted to intensive care unit and found that

66% had central hypotonia and 34% had peripheral causes.⁶

In the majority of studies, cerebral palsy is the most common cause of central hypotonia, while in our study the frequency of idiopathic central hypotonia was higher than cerebral palsy. This may be due to various reasons; in our country, specific genetic tests like FISH (flourescent insitu hybridization) method and molecular genetic testing are not available. In cases with abnormal facies and dysmorphology, gentic study has been limited to karyotype, as a result of which it is possible to mistakenly classify some of these cases in the idiopathic group. Again in our study, serum aminoacid chromatography was performed using the qualitative method, and we could not measure serum and urine organic acids, and some cases of inborn errors of metabolism may remain undiagnosed and classified in the idiopathic group.

In patients examined after three months of age, TORCH study (Toxoplasma, Rubella, Cytomegalovirus, Herpes simplex) was not reliable, because it could not differentiate between congenital and acquired infections; again some of these patients may have been classified in the idiopathic group. Birdi K et al,

could not find a clear etiology for hypotonia in 31% of their cases, indicating difficulty in determining the etiology in hypotonic infants and neonates who present with floppiness and hypomobility.¹¹ Some profile have been proposed for determination of the causes of infantile hypotonia but, to the best of our knowledge, none of them had good diagnostic value and were widely agreed upon.¹²⁻¹⁶ It is necessary to prepare an algorithm with high accuracy in order to facilitate determination of the etiology of hypotonia in infants and young children. It is also necessary in our country to constitute new diagnostic methods including specific genetic and metabolic tests.

CONCLUSIONS

In this study "central hypotonia" was most prevalent etiology of hypotonia. The most common cause of central hypotonia was idiopathic central hypotonia followed by cerebral palsy, brain structural abnormality, inborn errors of metabolism, genetic disorders and the TORCH syndrome.

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