Original Article

Causes &clinical presentation of hypotonia in children

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Summary:

Background: Hypotonia is not a specific medical disorder, but a potential manifestation of many different diseases and disorders. The long-term effects of hypotonia on a child's development and later life depend primarily on the severity of the muscle weakness and the nature of the cause.

Patients &Methods: A prospective, cross sectional descriptive study in which 62 patients with hypotonia, age 3months to13 years, were evaluated in children welfare teaching hospital /Baghdad (a tertiary care center), over 4months Period (1st of January to 1st of May,2008) . Children were categorized into groups of central , peripheral& systemic hypotonia, and specific diagnosis of each of groups was made by clinical findings, neuroimaging, metabolic, muscular enzymes, Electromyography-Nerve conduction velocity, thyroid function tests, Serum Calicium&X- RAY of left wrist,& TORCH (*Toxoplasmosis,others, rubella, CMV, herps simplex)* assay in our medical teaching laboratories.

Results: The most common cause of hypotonia was central in 30 patients (48.4 %). (Four patient with unknown causes), the most common lesion was brain atrophy detected by CT scan examination in 23/30 (76.7%). Peripheral causes found in 14/58 (22.6%) which include myopathies in 7 patients (11.3%), anterior horn cell lesion in 7 patients (11.3%). Systemic causes were found in 14/58 (22.6%). Early Onset in 46/62 (74.2%), while late onset constituted 16/62 (25.8%).The most common mode of presentation is delayed mile stones found in 32 patients (51.6%).

Conclusions: The most common cause of hypotonia in children enrolled in the study is central lesion and commonly occurs in pre natal, natal & post natal periods. The most common finding is brain atrophy diagnosed by CT scan, while the most common presentation is delayed milestones, and most common type of weakness is proximal.

Keywords Hypotonia, presentation, central, peripheral, onset.

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Introduction:

Hypotonia is a condition of abnormally low muscle tone (the amount of tension or resistance to movement in a muscle), often involving reduced muscle strength. Recognizing hypotonia, even in early infancy, is usually relatively straightforward, but diagnosing the underlying cause can be difficult and often unsuccessful. The long-term effects of hypotonia on a child's development and later life depend primarily on the severity of the muscle weakness and the nature of the cause. The principal treatment for most hypotonia of idiopathic or neurologic cause is physical therapy to help the person compensate for the neuromuscular disability (1).

Classification of hypotonia: A.according to site of damage. (2)I. Lesion in the Brain (central hypotonia)
1. Cerebral palsy A .Atonic B.Athetoid CP
2. Chromosomal abnormalities: (Prader-Willi syndrome)
3. Degenerative disease of brain
A. White matter. Metachromatic leukodystophyies (AR).
B.Gray matter. 1. Neiman-Pick disease 2. Kinky hair disease. 3. Tay-Sachs
II. Lesion in the spinal cord: Trauma.
III. Lesion in the Anterior Horn Cell: 1. Poliomyelitis 2.Pompe Disease 3. Spinal muscle atrophy. A. Acute infantile SMA, Type I (Werding-Hoffmann dis.). B. type II SMA C. Kugelberg-Welander disease
IV. Lesion in Peripheral Nerve: Guillain-Barre syndrome
V. Lesion in the Neuromuscular Junction:1.Botulism: 2.Neonatal myasthenia gravis:
VI. Lesion in Muscle: 1. Muscular Dystrophy 2.Myotonia dystrophy: 3. Congenital Myopathies: 4. Metabolic Myopathy
B.:classification of hypotoni according to onset of presentation.(1)
1. Genetic disorders are the most common causes a. Down's syndrome (most common) b. Achondroplasia c. Infantile spinal muscular atrophy such as Werding-Hoffman disease d. Marfan's syndrome e. Menkes syndrome f.Prader-Willi syndrome g.Tay-Sachs

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disease h. Cerebellar ataxia (congenital) i.Hypothyroidism j.(congenital) Hypotonic Cerebral palsy .
2. Acquired- i.e. onset occurs after birth. A. Genetic:1. Muscular dystrophy. 2. Metachromatic leukodystrophy B. Infection: Encephalitis, Guillian-Barre syndrome, Infantile botulism, Meningitis, Poliomyelitis, Sepsis. C. Autoimmunity disorder: a. Myasthenia gravis b. abnormal vaccine reaction D. Metabolic disorder (rickets, hypervitaminosis)
Evaluation:
Floppy infant: refers to an infant less than one year of age who is hypotonic & whose examination is characterized by the following: Display poor head control when pulled to a sitting position, landau reflex: Form the posture of a C when held in ventral suspension , lies in a frog leg position (abduction of legs, with lateral surface of the thighs on the table.) (2). And vertical suspensions test: infant is supported by examiners' hands in axilla there is tendency to slip through. The examination of these neonates is notable for aweak suck, feeble cry, &poor respiratory excursion. Not with draw from painful stimuli, there is little resistance to passive movement &the degree of movement excursion is often increasing (3). When evaluating a floppy infant, the first goal is to distinguish whether it is central or peripheral. Routine diagnostic procedures in suspected neuromuscular disorders include measurement of muscle enzyme activities, electroneurography and electromyography, genetic analysis, and if necessary, biopsies of muscles and nerves. (4-6)Modern imaging techniques such as sonography and magnetic resonance Imaging (MRI) allow non-invasive depiction of muscle anatomy and thus are being increasingly included in the diagnosis of neuromuscular disease(7).

Patients and methods:
A prospective cross- sectional study was performed in children welfare Teaching hospital, a tertiary care center in the period from the 1st of January 2008 to 1st of May 2008 . Children age ranged from 3mo. - 13 yr. whose predominant problem was hypotonia and had been clinically confirmed (head lag, Form the posture of a C when held in ventral suspension, vertical suspensions test: infant is supported by examiners' hands in axilla there is tendency to slip through…etc.) 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 cranioneuroimaging (CT scan or MRI) was carried out, 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 84 infants were included, with 22 of these being excluded from the final analysis because of the following: insufficient information, acute hypotonia. &age less than 3 mos. 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 test.
Statistical analysis: all data were coded & enter to tables by using statistic package for social sciences SPSS14. All data summarized by using: numbers, & percentages.

Results:
A total number of cases was sixty two with male to female ratio 1.69: 1, and age ranges from 3 mo. - 13 yr. Those floppy infants below 1year were (59.7%)& above one year were (40.3%) (Table 1&2) Early Onset in 46/62 (74.2%), while late onset constituted 16/62 (25.8%). (Table3). Most common causes were central found in 30/58 (48.4 %). (Four patient with unknown causes) (Table4). The most common lesion was brain atrophy detected by CT scan examination in 23/30 (76.7%) (Table5). Systemic causes were found in 14/58 (22.6%) (Table6). Proximal muscle weakness was commonest type of weakness found in 35/62 (56.5%). (Table 7).Spinal muscle atrophy (SMA type I) in 6/62 (9.7%), most common peripheral cause.(Table 8). Most common mode of presentation is delayed mile stones found in 32/62 (51.6%) in (table 9).

Table (1): Distribution of patients according to the

Age	**No.**	**Percent**
<1year	37	59.7%
> 1 year	25	40.3 %
Total	62	100%

Age:

Table (2): Distribution of patients according to the gender:

Gender		No.	Percent
	Male	39	62.9 %
	Female	23	37.1%
	Total	62	100.0%

Table (3): Distribution of patients according to onset:

ONSET		No.	Percent
	Early	46	74.2
	Late	16	25.8
	Total	62	100.0

Table (4): Distribution of patients according to site of lesion

Site		No.	%
	Brain	30	48.4%
	systemic	14	22.6%
	muscle	7	11.3%
	Anterior horn cell	7	11.3%
	Total	58	93.5%
	undetermined cause	4	6.5%
Total		62	100.0%

Table (5): Distribution of patients with central causes & mixed causes according to type of lesion in brain diagnosed by CT or MRI.

Type of brain lesion		No.	%(from Central)
	Brain atrophy	23	76.7 %
	White matter degeneration	5	16.7 %
	Gray matter degeneration	1	3.3 %
	Hydrocephaly	1	3.3%
	Total	30	100.0 %

Table (6): Distribution of patients with systemic hypotonia according to their causes:

Systemic causes		No.	%(from Systemic)
	TORCH	4	28.6 %
	Down syndrome	4	28.6%
	Rickets	5	35.7 %
	Hypothyroidism	1	7.1 %
	Total	14	100.0 %

Table (7): Distribution of patients according to presence of weakness & type of weakness:

Type of weakness		No.	%
	proximal	35	56.45
	Normal(no weakness)	20	32.25
	Distal	5	8.06
	Mixed(proximal, distal)	2	3.22
	Total	62	100.0

Table (8): Distribution of patients according to their EMG& NCV findings.

EMG & NCS		No.	Percent
	normal	48	77.4
	Spinal muscle atrophy type 1	6	9.7
	Congenital myopathies	3	4.8
	Muscle dystrophies	2	3.2
	Peripheral neuropathies	1	1.6
	Spinal muscle atrophy Type 3	1	1.6
	Duchene muscle dystrophy	1	1.6
	Total	62	100.0

Table (9): Distribution of patients according to mode of presentation:

Mode of presentation	No.	%
Delayed mile stones	32	51.6
Loss of attain stones	9	14.5
Chest infection	6	9.6
Seizure	6	9.6
Jaundice	5	8.0
Dysmorphic features	4	6.4
Total	62	100.0

Discussion:

This is the 1st study for patients with hypotonia carried out in the neurological out patient clinic &4th ward in Children Welfare Teaching Hospital /Baghdad. In this study, 39 male(62.9%) & 23 female (37.1%) were included, while in Amirsalari S1et al study, Forty six (45.8%) infants were male and fifty four(54.2%) were female (8), & in Albert E, et al study, Eighty-nine infants, 42 female (47.2%) and 47 male (52.8%), were included .(9). In this study,the most common cause of hypotonia was central , seen in 48.4 % of patients as in Nur Aydınlıa,et al. who found 41.4%(10)Results of Amirsalari S1et al study showed central hypotonia. In 101 patients (94.4%) and peripheral in four patients (3.7%) (8). In the Paro-Panjan D et al, study (11), they found that 88% of cases had central causes of hypotonia, 9% had peripheral causes and 3% remained undiagnosed, The study conducted by Eng GD in this aspect reported that 85% of cases had central causes and 15% had peripheral causes of muscle tone disturbance.(12).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. (13)In the majority of studies (8, 9, 10, 13), cerebral palsy is the most common cause of central hypotonia, which goes with this study results.In this study, brain atrophy by CT scan (mainly in patients with atonic cerebral palsy) constitute 23/30 patients (76.7%) with central hypotonia, white matter degeneration 5/30 (8.1%), gray matter degeneration1/30 (1.6%) , hydrocephaly was found in1/30 (1.6%) determined by CT or MRI,while in Nur Aydınlıa,et al study 5/12 patients (41.6%) had brain atrophy &other have structural brain anomalies. they use MRI that show more details. (10) In Amirsalari S1,et al study, the most common cause of central hypotonia was idiopathic central hypotonia 34 (31.8%), followed by cerebral palsy in 22 (20.6%), brain structural abnormality in 19 (17.8%), inborn errors of metabolism 14 (13.1%), genetic disorders 7 (6.5%) .(8) &In Albert E, et al study a, definitive diagnosis was established in 60 (67.4%) cases, in 24 cases (40%) on purely clinical grounds, whereas in 36 (60%) cases, additional investigations were necessary. Karyotype, molecular diagnostics, cranial imaging, and muscle and skin biopsy provided diagnostic information. Genetic disorders in 18/ 60 (20.2%), congenital or acquired disorders of the central nervous system in 22/60 (24.7%), and disorders of the lower motor unit in 9 / 60 (10.1%) contributed to the majority of diagnoses (9) In this study, the peripheral causes constitute 14/62 patients (22.6%) diagnose clinically & by EMG &NCS facility, lesion in anterior horn cell (A.H.C.) [6/62 (9.7%) have spinal muscle atrophy type I (werding Hofmann disease),1/62 (1.6%) has spinal muscle atrophy type 3 (late onset)]. Six out of sixty two patients (9.7%) have lesion in muscle, 1/62 (1.6%) have Duchene muscle dystrophy by EMG& proved by muscle biopsy, 2/62 patients (4.8%) have congenital myopathies & 2/62 (3.2%) have muscle dystrophies by EMG findings. Only one patient (1.6%) has peripheral neuropathy by NCS. while in Nur Aydınlıa,et al study, there are 58.5% with peripheral causes diagnosed by EMG&US of muscle, 15/41 patients (36.5%) have lesion, 6/41 patients (14.6%) have lesion in muscle& one patient (2.4%) has neuropathy.(10) Systemic causes were found in 14/58 (22.6%) which include Congenital infection (TORCH) 4/14 (6.5%) , While in Amirsalari S1et al study, TORCH(Toxoplasma,Rubella, Cytomegalovirus, Herpes simplex) syndrome in 3/14 (2.9%)(8) , Down syndrome in 4/14 (6.5%), Rickets in 5/14 (8.1%), &Hypothyroidism in1/14 (1.6%). In this study, birth asphyxia constitute (14.5%) of patients with central hypotonia While in Amirsalari S1, et al study, 24 patients with centeral hypotonia (23.8%) had a positive history of birth asphyxia (9), because our patients lack the documented medical recorded data about prenatal period &we detected birth asphyxia from the history. In this study, the spinal muscle atrophy type I was the most common and accounts for (85.6%), which is similar to Grohmann K, et al study 96% (14) .

Conclusion:

Most common causes of hypotonia are central **(**lesion in brain),most common lesion is brain atrophy diagnosed by CT, MRI, most common mode of presentation is delayed mile stones,the onset commonly occurs early and SMA type 1 (werding Hoffman disease) was the most common muscle disease.

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