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Review article in

Cerebral palsy

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Introduction

Cerebral palsy (CP) is a neurodevelopmental condition that affects muscle tone, movement and motor skills. This is not a single disease but rather a heterogeneous clinical syndrome resulting from injury to the developing brain. Although the disorder itself is non-progressive, the clinical expression changes over time as the brain matures [(1)].

The current definition of CP, as adopted by the International consensus in 2005 is [(2)] '*Cerebral palsy describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain'*. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior, by epilepsy and by secondary musculoskeletal problems.

Basically, it is a static encephalopathy with a delayed developmental presentation. Although it may appear to worsen, changes are actually the result of the deficits becoming more obvious as the child grows and matures over time. The area of the brain affected or damaged is directly reflected by the resulting disabilities. Although it is a motor disorder, it also can be associated with additional developmental disabilities, such as cognitive impairment, depending on the degree of brain damage that has occurred. There is no cure for this lifetime condition, but therapy, education, and technology can maximize each child's potential by improving functional abilities and quality of life [(3)].

CP is characterized by heterogeneity in risk factors, underlying specific etiology, clinical features, severity of functional limitations, associated

and secondary conditions, treatment options, and evolution of the condition over the lifespan of the individual [4]. The prevalence of CP for all live births ranges from 1.5 to 3 per 1,000 live births, with variation between high income and low to middle income countries and geographic region [5]. Because, in many infants and children, abnormal neuromotor findings tend to resolve within the first few years, especially during the first 2–5 years, of life, the reported prevalence of CP tends to be higher during infancy. Although prematurity and low birthweight are main risk factors for CP, multiple other factors are also associated with or potentially increase the risk for CP [6].

In this short review, we will demonstrate the etiology, risk factors, clinical features, diagnosis and possible therapeutic strategies of the cerebral palsy.

Prevalence

Estimates of CP prevalence in the 21st century, however, reveal a mixed picture. During the first decade of the century, estimates of CP prevalence were generally higher than in the 20th century in high-income countries (HICs). In the USA, prevalence estimates increased from 2 to as high as 3 cases per 1,000 live births between 2002 and 2012, although the most recent of these surveys showed a slight decline to 2.9 per 1,000 8-year-old children in 2010 from 3.5 in the same surveillance area in 2006. However, studies in Australia, Europe, Canada, Sweden and Japan have provided evidence for a declining prevalence of CP over time, mostly among low-birthweight and preterm infants [7]. In China, a decline from 1.6 to 1.25 cases per 1,000 children between 1999 and 2017 has been reported, although ascertainment methods for these

reports might have differed from the long-standing registers used in Australia and Europe [8].

Etiology

The etiology of CP is very diverse and multifactorial. The causes are congenital, genetic, inflammatory, infectious, anoxic, traumatic and metabolic. The injury to the developing brain may be prenatal, natal or postnatal. As much as 75% - 80% of the cases are due to prenatal injury with less than 10% being due to significant birth trauma or asphyxia [9]. According to study conducted in 2016, The most common etiologies included intrapartum hypoxic events (18%), prematurity (15%) and postnatal infections (15%), followed by focal ischemic stroke (10%) and prenatal infections (10%). (3%) had cerebral palsy secondary to kernicterus and (3%) had congenital brain malformations and the remnant percentage where idiopathic [10]. Perinatal risk factors include multiple pregnancies, with significantly increased risk for CP. Twin pregnancies result in a child with CP about 12 times more than a single pregnancy, probably related to a low birth rate. Brain hemorrhage during delivery, other types of birth trauma, kernicterus, vaginal bleeding on admission, placental complications, hypoxia, and anoxia were all associated with increased rate of CP. Postnatal causes include head trauma, meningitis, encephalitis, and brain infarcts. Genetic causes that are known to be a risk factor for CP involve a gene on chromosome 19 [11].

Pathophysiology

During the first trimester of pregnancy until 24 weeks of gestation, the development of cortical neurogenesis occurs which is characterized by organization, migration, and proliferation of precursor cells of neurons.

This can be affected by genetic deficits, infections, or toxic agents resulting in malformations like lissencephaly, polymicrogyria, cortical dysplasia, and schizencephaly. In the second phase of pregnancy, growth, and developmental events like axonal and dendrite growth, myelination, synapse formation takes place. At this stage of brain development environmental factors like ischaemia, hypoxia is involved and causes CP. The CP is the result of impaired and destructive developmental mechanisms [12]. Interaction of several causal factors causes CP but the pathophysiological mechanism is common in CP. Hypoxic–ischaemic and inflammatory conditions are the key factors that cause cell death or loss of cell processes. They produce pro-inflammatory cytokines in excess, cause oxidative stress, modification of extracellular matrix, deprivation of growth factors, and excessive release of glutamate thus triggering the excitatory cascade reactions. These processes result in myelination gliosis defects, degeneration of thalamus involving secondary cortical and maldevelopment of thalamus in preterm newborns. After any injury, the microglial cells are the first elements that respond. These cells mediate neurotoxicity because of the expression of both ionotropic and metabotropic, adenosine and glutamatergic receptors involved in inflammatory responses [13]. Axonal injury and degeneration have been observed in the focal necrotic component and the diffuse component of human white matter injury. Moreover neuronal death and gliosis are common in the subplate, the basal ganglia, and the cerebellum. Neuronal loss of GABAergic neurons in the subplate has been noted in autopsy studies of human preterm newborns with periventricular leukomalacia. Contrary to thalamic and basal ganglia neurons, which are vulnerable and often damaged, cortical layer neurons are still immature and less sensitive to hypoxic injuries [14].

Classification of CP

The information available to provide an adequate classification of the features of CP in any individual will vary over the age span and across geographic regions and settings. The role of aging in changing the clinical phenomenology of CPhas been little studied, and the possibility of classification changes over time cannot be completely dismissed. Table 1 demonstrate the most common used system of classification [15].

Table 1. Classification of CP

1. Motor abnormalities A. NATURE AND TYPOLOGY OF THE MOTOR DISORDER: The observed tonal abnormalities assessed on examination (e.g. hypertonia, hypotonia) as well as the diagnosed movement disorders present, such as spasticity, ataxia, dystonia, athetosis. B. FUNCTIONAL MOTOR ABILITIES: The extent to which the individual is limited in his or her motor function, including oromotor and speech function.
2. Accompanying impairments The presence or absence of later-developing musculoskeletal problems and/or accompanying non-motor neurodevelopmental or sensory problems, such as seizures, hearing or vision impairments, or attentional, behavioral, communicative and/or cognitive deficits, and the extent to which impairments interact in individuals with cerebral palsy.
3. Anatomical and neuro-imaging findings A. ANATOMIC DISTRIBUTION: The parts of the body (limbs, trunk, bulbar region, etc.) affected by motor impairments or limitations. B. NEURO-IMAGING FINDINGS: The neuroanatomic findings on CT or MRI imaging, such as ventricular enlargement, white matter loss or brain anomaly.
4. Causation and timing Whether there is a clearly identified cause, as is usually the case with post-natal CP (e.g. meningitis, head injury) or when brain malformations are present, and the presumed time frame during which the injury occurred, if known.

Clinical features

Seventy to 80 percent of patients with cerebral palsy have spastic clinical features. Affected limbs may demonstrate increased deep tendon reflexes, tremors, muscular hypertonicity, weakness, and a characteristic scissors gait with toe-walking. The athetoid or dyskinetic type of cerebral palsy, affecting 10 to 20 percent of patients, is characterized by abnormally slow, writhing movements of the hands, feet, arms, or legs that are exacerbated during periods of stress and absent during sleep. The rarest form, ataxic cerebral palsy, affects 5 to 10 percent of patients and predominately impairs balance and coordination. These patients walk with a wide-based gait and have intention tremors that complicate performance of daily activities requiring fine-motor function [(16)]. Intellectual impairment occurs in about two thirds of patients with cerebral palsy. About one half of pediatric patients have seizures. Children with CP grow less well than their neurologically normal peers. The contribution of specific brain injury does not fully explain growth faltering in children with CP. The pattern of early growth failure in CP suggests chronic undernutrition. Body mass is gradually lost, followed by faltering linear growth with subsequent drop-off in head growth [(17)]. There are three predominant CP syndromes (spastic, dyskinetic and ataxic).

CP can be classified according to the topographic distribution of motor involvement. Motor deficits include [(18)]: monoplegia, diplegia, hemiplegia, triplegia, quadriplegia, and double hemiplegia.

Diplegia is present when the lower extremities are primarily affected, although the upper extremities are not completely spared. Spastic diplegia is the most common type of CP and is associated with prematurity. The periventricular germinal matrix, which is a region of active neuronal

proliferation, is particularly susceptible to bleeding and hypoxic ischemic injury. Hemiplegia is characterized by involvement of one side of the body, with the arm typically more affected than the leg. This is because of larger cortical representation (motor homunculus) of the hand and arm compared to a smaller leg area. Monoplegia refers to single limb involvement. This is usually the result of very mild hemiplegia with arm deficits only. when all four limbs are involved, quadriplegia is the appropriate descriptive term. This is the most disabling, with 25% of the affected children requiring total care. Double hemiplegia refers to the child with quadriplegia involving the arms more than the legs with side asymmetry [(18)].

Management

The physiotherapist and occupational therapist have central roles in enhancing motor control in the child with CP. PT is the mainstay of management for the motor deficits in CP, focusing on gross motor skills and functional mobility. Positioning, sitting, transition from sitting to standing, walking with or without assistive devices and orthoses, wheelchair use and transfers, are areas that the physiotherapist works on. In clinical practice variations exist in methods of evaluation and in treatment decisions; these differ with age, function of the child and the family's needs. Therapeutic methods, frequency and duration of service, settings and service delivery system vary. Variations in management practices combined with the lack of clear scientific evidence demonstrating the benefits of the interventions and poor reporting of available research have clinical implications [(19)]. Physiotherapy especially when started early in life, is helpful in promoting normal motor development, and preventing deformityand contractures. In the young child it aims at reducing abnormal patterns of movement and posture and promoting the normal ones so as to enable the child to gain maximal

functional The most popular traditional method used for the purpose of reducing abnormal patterns of movement and posture and promoting the normal ones in order to gain maximal functional independence, is the Bobath approach, known as NDT. Based on reflex hierarchical theory, NDT aims to normalize the muscle tone, inhibit primitive and abnormal reflexes and facilitate normal movements [20]. The use of botulinum toxin type A BoNT-A has become a 'standard of care' for children with CP in many countries, leading to widespread clinical use and the publication and dissemination of consensus statements. The most frequent indication for BoNT-A therapy in CP is to treat focal muscle over-activity to improve gait and function in children who can walk. Injection of the upper limb to improve posture and function is the second most frequent indication for BoNT-A therapy in children with CP [21]. The only indication for BoNT-B is resistance to BoNTA caused by the presence of neutralising antibodies. The vast majority of clinical studies in children with CP have been with the various preparations of BoNT-A, principally onabotulinum toxin A (Botox®) and abobotulinum toxin A (Dysport®). Injection of BoNT-A produces a dose-dependent, partially reversible chemo-denervation of injected muscle by blocking pre-synaptic release of acetylcholine at the neuromuscular junction [22]. Intrathecal baclofen (ITB) was approved for the treatment of spasticity of cerebral origin in 1996. ITB was shown to be beneficial in dystonic CP, although not in other dyskinetic forms of CP. Further investigation is warranted for the effect of ITB in the dystonic CP, including description and assessment of dystonic CP. An improvement in the quality of the upper limb function was also shown. Improvements in positioning, transfers, dressing, toileting/hygiene and comfort were reported; cost-effectiveness of ITB was confirmed for carefully selected children with intractable spastic CP [23]. Surgery is mainly undertaken on the lower limb, but occasionally in

the upper limb. Some children require surgery for scoliosis. Physiotherapy is an essential part of post-operative management. Gait laboratories are useful in planning the surgical program for children who can walk independently or with sticks or walking frames [24].

Conclusion

CP is a common neurodevelopmental disorder that affect a lot of children around the world. the children live abnormal live because their lack motor abilities and face a lot of hardships socially and mentally and they need very special emotional and parental support to live normally. The need for more attention and care for this group increased in the last decades and this make an obligation for the authorities to provide special centers for CP patients health care and give appropriate training for the staffs about how to deal with these patients.

References

1. Gulati S, Sondhi V. Cerebral palsy: an overview. The Indian Journal of Pediatrics. 2018 Nov 1;85(11):1006-16.
2. The Definition and Classification of Cerebral Palsy. Dev Med Child Neurol. 2007;49:1–44.
3. Jones MW, Morgan E, Shelton JE, Thorogood C. Cerebral palsy: introduction and diagnosis (part I). Journal of Pediatric Health Care. 2007 May 1;21(3):146-52.
4. Patel DR, Greydanus DE, Calles Jr JL, Pratt HD. Developmental disabilities across the lifespan. Disease-a-month. 2010 Jun 1;56(6):304-97.

5. Stavsky M, Mor O, Mastrolia SA, et al. Cerebral palsytrends in epidemiology and recent development in prenatal mechanisms of disease, treatment, and prevention. Front Pediatr 2017;5:21.

6. Graham HK, Rosenbaum P, Paneth N, Dan B, Lin JP. Damiano DL et al. Cerebral palsy. Nat. Rev. Dis. Primers. 2016;2:15082.

7. Durkin, M. S. et al. Prevalence of cerebral palsy among 8-year-old children in 2010 and preliminary evidence of trends in its relationship to low birthweight. Paediatr. Perinat. Epidemiol. 30, 496–510. 2016

8. He, P., Chen, G., Wang, Z., Guo, C. & Zheng, X. Children with motor impairment related to cerebral palsy: Prevalence, severity and concurrent impairments in China. *J. Paediatr. Child Health* **53**, 480–484 (2017).

9. Sankar C, Mundkur N. Cerebral palsy-definition, classification, etiology and early diagnosis. The Indian Journal of Pediatrics. 2005 Oct;72(10):865-8.

10. Bearden DR, Monokwane B, Khurana E, Baier J, Baranov E, Westmoreland K, Mazhani L, Steenhoff AP. Pediatric cerebral palsy in Botswana: etiology, outcomes, and comorbidities. Pediatric neurology. 2016 Jun 1;59:23-9.

11. Bialik GM, Givon U. Cerebral palsy: classification and etiology. Acta Orthop Traumatol Turc. 2009 Mar 1;43(2):77-80.

12. Marret S, Vanhulle C, Laquerriere A. Pathophysiology of cerebral palsy. *Handbook Clin Neurol*. 2013;111:169-176.

13. Upadhyay J, Tiwari N, Ansari MN. Cerebral palsy: Aetiology, pathophysiology and therapeutic interventions. Clinical and Experimental Pharmacology and Physiology. 2020 Dec;47(12):1891-901.

14. Marret S, Vanhulle CA, Laquerriere AN. Pathophysiology of cerebral palsy. Handbook of clinical neurology. 2013 Jan 1;111:169-76.

15. Rosenbaum P, Paneth N, Leviton A, Goldstein M, Bax M, Damiano D, Dan B, Jacobsson B. A report: the definition and classification of cerebral palsy April 2006. Dev Med Child Neurol Suppl. 2007 Feb 1;109(suppl 109):8-14.

16. Taylor F, National Institute of Neurological Disorders and Stroke (U.S.), Office of Science and Health Reports. Cerebral palsy: hope through research. Bethesda, Md.: The Institute, 2001. Accessed online September 28, 2005

17. Andrew MJ, Sullivan PB. Growth in cerebral palsy. Nutrition in Clinical Practice. 2010 Aug;25(4):357-61.

18. Cooper J, Majnemer A, Rosenblatt B, Birnbaum R. The determination of sensory deficits in children with hemiplegic cerebral palsy. J Child Neurol. 1995;10:300–9.

19. Anttila H, Malmivaara A, Kunz R, Autti-Ramo I, Makela M. Quality of reporting of randomized, controlled trials in cerebral palsy. Pediatrics 2006;117:2222–30.

20. Papavasiliou AS. Management of motor problems in cerebral palsy: a critical update for the clinician. european journal of paediatric neurology. 2009 Sep 1;13(5):387-96.

21. Multani I, Manji J, Hastings-Ison T, Khot A, Graham K. Botulinum toxin in the management of children with cerebral palsy. Pediatric Drugs. 2019 Aug;21(4):261-81.

22. Jankovic J. Botulinum toxin: state of the art. Mov Disord. 2017;32(8):1131–8.

23. Mess SA, Kim S, Davison S, *et al*. Implantable baclofen pump as an adjuvant in treatment of pressure sores. Ann Plast Surg.2003;51(5):465-7.

24. Padmakar S, Kumar KS, Parveen S. Management and Treatment for Cerebral Palsy in Children. Indian Journal of Pharmacy Practice. 2018 Apr;11(2):104-9.