REVIEW ARTICLE

A Review on the Types, Risk Factors, Diagnosis, and Treatment of Cerebral Palsy

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Abstract

Introduction: Cerebral palsy (CP) is the principal cause of disability in children. It is a neuromuscular disease that occurs due to the lesion in the infant's cerebral motor cortex that is acquired before, at, or within 5 years of birth.

Aim and objective: The purpose of this review is to inform the persons who are working on rehabilitation services, doctors, and well-wishers of disabled children to reduce their problems by diagnosing the type of CP and by using suitable bioactive molecules, antioxidants, chemicals, and different therapies.

Materials and methods: Eligible articles of various journals which are obtained from the Internet were studied very carefully to establish the results of types, risk factors, diagnosis, and the management of CP.

Results: Total 76 reviews or research-based journal articles were reviewed. Among them, 28 were correlated with diagnosis, 7 were related with risk factors, 6 were associated with diagnosis, 20 were linked with the prevention, and the rest 15 articles were connected with the introductory part of CP.

Conclusion: The findings of this article emphasize describing the types, risk factors, types, correct diagnosis methods, and treatment processes of CP.

Keywords: Antioxidants, Cerebral palsy, Diagnosis, Paralysis, Therapy.

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Introduction

Cerebral palsy (CP) is an umbrella term that covers a broad area of cerebral disorders which is the result of motor impairment that occurs in childhood. For the convenience of application, this term is used for a group of motor disorders of central origin defined by clinical explanation.[1] It is one of the most frequently recorded causes of early death.[2] It is a neurodevelopmental disorder that may occur during the development of the fetus, during or after birth. This is characterized by abnormalities of muscular tonicity, fine motor skills, gross motor skills, and causes injury to the progressing brain.[3] Disturbances in the walk, cognition, growth, sense, etc., are also found in the patients suffering from this disorder.[4] The first medical description of CP in the ancient world was made by Hippocrates in his work "Corpus Hippocraticum".[5] Enormous study of CP was conducted in the 19th century by William John Little and after that spastic diplegia was named as "Little's disease".[5] From German *zerebrale Kinderlahmung* which means cerebral child-paralysis, William Osler has first named this disorder as "cerebral palsy".[6] The signs and symptoms alter among people and over time.[7] The children suffering from CP are frequently exhibited cognitive and sensory impairments, epilepsy, and nutritional deficiencies. The patient may be suffering from different types of problems with sensation, vision, hearing, swallowing, and talking.[7] The babies with CP mostly do not roll over, sit, creep, or walk as similar as other children can do of the same ages.[7] With the other symptoms which occur one-third of the persons suffering from CP consist of seizures and trouble with thinking or reasoning.[7] The study of Odding et al.[8] expresses that this disorder is strongly associated with hemiplegia and diplegia. It is the commonest physical disability in the early days of life which takes place in 2.0–2.5 numbers among 1,000 live births.[9] Prevalence of CP is significantly connected with lower education status and it has been suggested to be less common in high-income countries than the low-income or middle-income countries.[10] Populations with high income have revealed a reduced life expectancy in children with CP, predominantly in children with severe motor and eating impairments and a decreased occurrence with age has been observed in China and India.[10–12] Only about a 40% chance of living to age 20 of a child of 2-years-old who is suffering severe CP in respect to a child of mild CP whose chance is 99%.[2] The diagnosis of CP in contrast includes metabolic and genetic disorders.[4] Blair and Watson expressed that the definition of CP is determined depending on the three general characteristics like body movement or posture disorder, static abnormality in the brain, and acquired brain disorder in early life.[13] Though, these characteristics do not indicate the properties like the strength of the movement disorders, static nature of the cerebral abnormality, the age when the abnormality takes place, and the age before which CP was not detected.[13] The most important risk factors are low birth weight, intrauterine infections, and multiple gestations

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for this disorder.[14] Cerebral palsy has a significant impact on the well-being of a family and societal health care costs.[15]

Types of Cerebral Palsy

Three main types of CP are spastic, dyskinetic, and ataxic type.[16] But based on the motor disability, the CP is divided into four main categories, namely spastic (pyramidal), athetoid or dyskinetic, ataxic, and mixed form.[17] If different types of characteristics of all three main types of CP are present in an individual then it is considered as a mixed type of CP. The most common type of this disorder is spastic type[16,18] followed by athetoid or dyskinetic, and ataxic type of CP.[16] According to spastic CP is affecting approximately 87% of children with CP.[16]

Spastic (Pyramidal) Cerebral Palsy

Spastic type of CP is very common among patients who are suffering from CP.[19] The patients with spastic CP are hypertonic with stiff, tight muscles which cannot relax in some parts of their body and the affected joints can become rigid in their body which provides difficulty to move.[20–22] Hip adductor spasticity leads to discomfort, stiffness, and difficulties in doing physical activities such as sitting, transfer, and walking.[19] Reduced volume of muscle, cross-sectional area, muscle length, and increased subcutaneous fat is found in the children suffering from spastic diplegic CP with gross motor function classification system II significantly compared with typically developing children.[20] The diagnosis of this disorder in the early stage still remains a challenge. In the case of infants, lesions in the corticospinal tract play a vital function in a motor impairment which is related to spastic CP with periventricular white matter injury.[23] People who are suffering from spastic CP struggle to control their movements, drink, eat, and speak.[24,25] Walk with an abnormal gait, like walking depending on their toes instead of on their flat feet in many people with such disorder.[26]

Spastic CP has been split into three categories:

- Spastic hemiplegia: In this type of CP, the leg, arm, and hand are on one side of the body.[27] Spastic hemiplegia or unilateral CP is the state of a person where muscle control and function on one side of the body of the patient is affected. The children of this disorder facing difficulties while using their hands collectively secondary to troubles that occur in the developing fetal or infant brain.[28]
- Spastic diplegia: Spastic diplegia is the most common form of CP which is found in the world.[29] Muscular rigidity, primarily in the legs is common in the disorder.[30] It presents a symmetric association of the lower limbs and upper limbs. Problems with motor control, spasticity, and balance which lead to gait abnormalities are frequently experienced by children with spastic diplegia.[31]
- Spastic quadriplegia: Most severe type of CP. It onsets when there are major malfunctioning of the brain.[32] In children with spastic quadriplegia, also described as "whole body involvement", spasticity can interfere with motor activities, is involved in the development of deformities, and adversely impacts care, positioning, and comfort.[33]

Athetoid or Dyskinetic Cerebral Palsy (ADCP)

This type of CP is the second most common type of CP after the spastic forms.[34] It occurs due to the malformation or damage extrapyramidal tracts in the basal ganglia or the cerebellum and is frequently related to severe handicap in movement and its treatment is very tough.[34,35] Athetoid or dyskinetic cerebral palsy is characterized by irregular postures or movements related to impaired tone regulation or movement coordination.[34] It is also associated with various motor disorders which are characterized by alterations in muscle tone and posture, with an altering element of involuntary movements.[36] Two major movement disorders namely dystonia and choreoathetosis occur at the same time in most cases, although some differences may occur.[37]

Ataxic Cerebral Palsy

Ataxic CP refers to a lack or loss of coordination in movement caused due to damage to cerebellar structures and is different from the other types of CP, namely spastic CP (damage to cortical motor areas and underlying white matter) and athetoid CP (damage to basal ganglia).[38] This is related to the injury or dysfunction of the cerebellum or its afferent and efferent projections.[39] This type of CP accounts for 5–10% among all types of CP and approximately 50% of ataxic CP is inherited as an autosomal recessive trait.[40] Ataxic diplegia and simple ataxia are the further subdivisions of ataxic CP which are characterized based on the presence or absence of spasticity in the lower limbs.[41] Cerebellum is very much significant for the coordination of muscular activities and body balance, so the patients with ataxic CP experience problems in coordination, specifically in their arms, legs, and trunk due to damaged cerebellum. Decrease muscle tone also occurs due to ataxic CP.[42]

Etiology and Risk Factors of Cerebral Palsy

Etiology of children CP can be resolute by looking back in some children includes multiple etiological factors which are related with parental, intrapartal, and postnatal causes which are as follows.[43–49]

Prenatal Causes

- Diseases like hypothyroidism, diabetes, viral illness, preeclampsia, etc., of the mother during pregnancy.
- Established inborn infections like toxoplasmosis, cytomegalovirus, rubella, herpes simplex, and others.
- If CP is present in brother-or-sister.
- Inherited disorders.
- Cerebral anomalies.
- Vascular blockages lead to the formation of intrauterine brain ischemia.
- Rh dissimilarity of the blood of mother and fetus.
- Pregnancy multiple times.
- Premature birth of a baby.

Intrapartal Causes

- Intrapartal hypoxia of the brain.
- Hypoxemia (asphyxia, apnea, respiratory insufficiency).
- Asystole, bradycardia, heart failure, circulatory failure in the sepsis, or other causes which leads to intrapartal brain ischemia.
- Bleeding inside the cranium.
- Hypoxic-ischemic encephalopathy.
- Focal periventricular leukomalacia.

Postnatal Causes

- Necrosis of subcortical cerebral region.
- Neonatal hypoglycemia.
- Encephalitis.

- Problems of acute metabolic crisis like hyperbilirubinemia, hypoxia, hypernatremia, and dehydration.
- Standardized brain hemorrhage (traumatic and non-traumatic).[43–49]

Diagnosis of Cerebral Palsy

After the first or second year of birth, CP usually is diagnosed. The early detection and diagnosis of CP comprise numerous measures of the underlying brain abnormalities and their neurodevelopmental consequences.[50] Different types of CP are often diagnosed based on the study of unusual muscle tone or posture, delayed motor milestones, or the occurrence of gait abnormalities in young children, which vary from mild, i.e., from toe-walking, to severe, which means crouched, internally rotated gait.[51] Brain imaging tests, such as computed tomography (CT scan)[52] or magnetic resonance imaging (MRI),[53] electroencephalogram (EEG),[54] genetic testing,[55] or a combination of these are suggested by specialists to detect different types of CP.

Prevention of Cerebral Palsy

Caffeine is a type of therapy that is capable to decrease the risk of CP in the preterm infants of a multicenter trial, but postnatal steroids, which are used in them to reduce lung inflammation and to diminish the risk of bronchopulmonary dysplasia, increases the risk of CP.[56] The risk of CP is extremely reduced in infants with low birth weight due to the administration of caffeine.[57] Dipeptide amides and peptidomimetics compounds which are built on L-N^{ω}-nitroarginine scaffold compounds can distribute readily to the fetal brain inhibit NOS activity and decrease NO concentration and show a significant defense to the fetal rabbit kits from the hypoxia-ischemia induced phenotype of CP.[58] The antioxidant melatonin has very effective to reduce the formation of free radicals in acute neonatal hemorrhagic brain injury which leads to the onset of mental retardation and CP.[59] Inhalation of hydrogen gas is a very successful strategy to protect the brain of an infant from the post-hemorrhagic reverberations of brain atrophy, mental retardation, and CP.[60] The result of multiple interacting risk factors instead of a single reason is CP and the administration of antenatal magnesium sulfate alone in preterm infants can prevent all cases of this illness. The primary prevention of CP in preterm infants who are <34 weeks of gestational age could be done by the use of this drug.[61]

Perinatal white matter injury or periventricular leukomalacia is a major cause of CP located in the survivors of premature infants.[62] Agomelatine (S 20098) is a melatonin derivative which is conducting its function through melatonin receptors.[63] The study of Gressens et al. concludes that it is a new promising drug to treat human periventricular leukomalacia and on neuroplasticity, it has beneficial effects.[63] Cell-based therapy by oligodendrocyte precursor cell (OPC)-transplantation demonstrates a potential protective effect on a subchronic model of periventricular leukomalacia. Investigation of Girard et al. showed that systemic administration of interleukin-1 receptor antagonist (IL-1Ra) has therapeutically potential to protect the brain in the animal model of perinatal brain injury using the insults which are most common to human neonates, i.e., prenatal exposure to inflammation and/or postnatal hypoxia-ischemia (HI).[64] The findings of Wei et al. suggest that bioactive factors like IGF-1 and BDNF are secreted by adipose-derived stem cells (ASCs), which protect the neurons of neonatal rats against brain damage induced by hypoxic ischemia in both *in vitro* and *in vivo*.[65] The observations of Fantacci et al. expressed that the administration of neurotrophins, like nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and glial-derived neurotrophic factor (GDNF), participate a crucial role in the development, differentiation, and active existence of the nerves of the central and peripheral nervous system, seem to be effective in helping to prevent neuronal loss and brain damage after hypoxic-ischemic brain injuries which may lead to CP.[66]

The first-line medication to combat dystonia in people with CP is the oral administration of trihexyphenidyl, often used by clinicians.[67] The study of Li et al. expressed that lithium mitigates brain injury by reducing apoptosis and autophagy after neonatal hypoxia-ischemia. Hypoxic-ischemic encephalopathy is related to the progression of CP and cognitive disability later in life.[68] Allopurinol is a xanthine oxidase inhibitor that reduces the free radical formation and counteracts hypoxia-reperfusion brain damage. Maternal administration of allopurinol just earlier to delivery both in animal and human studies of suspected intrauterine hypoxia suggest it counteracts hypoxic-ischemic encephalopathy.[69] Administration of atropine sulfate sublingually suggests it is very much effective to treat drooling in children and adolescents with CP.[70] Treatment of botulinum toxin type A to the patients who are suffering from hemiparesis and spastic paraparesis shows improvement by increase arches of mobility and functionality of the gait of the patients.[71]

A study by Gonnade et al. suggested that both the botulinum toxin type A and phenol protect children who are suffering from CP but phenol is comparatively safe and cheap.[72] Botulinum toxin type A in combination with physical and occupational therapy and neuromuscular electrical stimulation shows the advantageous result to the spastic upper limb of children with CP.[18] Hippotherapy affects the body functions, activities, and participation of the children suffering from CP and positively affects gross motor function and balance to them on different functional levels.[73] Neurodevelopmental treatment-based posture and balances training for 8 weeks protect the children with diparetic and hemiparetic CP by improving the functional motor level and functional independence by improving postural control and balance.[74] Orthotic devices which are called ankle-foot orthoses (AFOs) are used the children who are suffering from CP to standardize the walking pattern of children with CP. A target of orthotic supervision is to facilitate a more common walking pattern by positioning the joints in a suitable arrangement to trim down pathological response or spasticity. So, the use of unambiguous types of AFOs advances gait parameters, including ankle and knee range of motion, speed of walking, and the length of step and they decrease energy utilization in the suffering children with spastic CP.[75]

Conclusion

Cerebral palsy is a group of nonprogressive disorders, affects body movement and posture. It occurs during embryonic development or in early life. Types of this disorder with their diagnosis, risk factors, and treatment procedures are recapitulated in this review paper. Involvement approaches, hippotherapy, neurodevelopmental treatments, stem cell therapy, use of magnesium sulfate, allopurinol, melatonin, etc., appear promising to combat the problems which arise due to CP.

References

1. Badawi N, Watson L, Petterson B, et al. What constitutes cerebral palsy? Dev Med Child Neurol 1998;40(8):520–527. DOI: 10.1111/j.1469-8749.1998.tb15410.x.
2. Hutton JL. Cerebral palsy life expectancy. Clin Perinatol 2006;33(2):545–555. DOI: 10.1016/j.clp.2006.03.016.
3. Byrne R, Noritz G, Maitre NL, et al. Implementation of early diagnosis and intervention guidelines for cerebral palsy in a high-risk infant follow-up clinic. Pediatr Neurol 2017;76:66–71. DOI: 10.1016/j.pediatrneurol.2017.08.002.
4. Karen WK. Cerebral palsy: an overview. Am Fam Physician 2006;73:91–100.
5. Panteliadis C, Panteliadis P, Vassilyadi F. Hallmarks in the history of cerebral palsy: from antiquity to mid-20th century. Brain Develop 2013;35(4):285–292. DOI: 10.1016/j.braindev.2012.05.003.
6. Camilli A, Jenkner F, Lena G. Contribution to the study of the etiopathogenesis of cerebral palsy in children, by means of analysis of perinatal mortality. Arch Ital Pediatr Pueric 1967;25(1):17–22.
7. Haak P, Lenski M, Hidecker MJC, et al. Cerebral palsy and aging. Dev Med Child Neurol 2009;4:16–23. DOI: 10.1111/j.1469-8749.2009.03428.x.
8. Odding E, Roebroeck ME, Stam HJ. The epidemiology of cerebral palsy: incidence, impairments and risk factors. Disabil Rehabil 2006;28(4):183–191. DOI: 10.1080/09638280500158422.
9. Reddihough DS, Collins KJ. The epidemiology and causes of cerebral palsy. Aust J Physiother 2003;49(1):7–12. DOI: 10.1016/s0004-9514(14)60183-5.
10. Banerjee TK, Hazra A, Biswas A, et al. Neurological disorders in children and adolescents. Indian J Pediatr 2009;76(2):139–146. DOI: 10.1007/s12098-008-0226-z.
11. Day SM, Reynolds RJ, Kush SJ. Extrapolating published survival curves to obtain evidence-based estimates of life expectancy in cerebral palsy. Dev Med Child Neurol 2015;57(12):1105–1118. DOI: 10.1111/dmcn.12849.
12. Liu JM, Li S, Lin Q. Prevalence of cerebral palsy in China. Int J Epidemiol 1999;28(5):949–954. DOI: 10.1093/ije/28.5.949.
13. Blair E, Watson L. Epidemiology of cerebral palsy. Semin Fetal Neonatal Med 2006;11(2):117–125. DOI: 10.1016/j.siny.2005.10.010.
14. Gibson CS, MacLennan AH, Goldwater PN. Antenatal causes of cerebral palsy: associations between inherited thrombophilias, viral and bacterial infection, and inherited susceptibility to infection. Obstet Gynecol Surv 2003;58(3):209–220. DOI: 10.1097/01.OGX.0000055205.21611.6E.
15. Shankaran S. Prevention, diagnosis, and treatment of cerebral palsy in near-term and term infants. Clin Obstet Gynecol 2008;51(4):829–839. DOI: 10.1097/GRF.0b013e3181870c35.
16. Sellier E, Platt MJ, Andersen GL, et al. Decreasing prevalence in cerebral palsy: a multi-site European population-based study, 1980 to 2003. Dev Med Child Neurol 2016;58(1):85–92. DOI: 10.1111/dmcn.12865.
17. Elia AE, Bagella CF, Ferré F, et al. Deep brain stimulation for dystonia due to cerebral palsy: a review. Eur J Paediatr Neurol 2018;22(2):308–315. DOI: 10.1016/j.ejpn.2017.12.002.
18. Rodríguez-Reyes G, Alessi-Montero A, Díaz-Martínez L, et al. Botulinum toxin, physical and occupational therapy, and neuromuscular electrical stimulation to treat spastic upper limb of children with cerebral palsy: a pilot study. Artif Organs 2010;34(3):230–234. DOI: 10.1111/j.1525-1594.2009.00768.x.
19. Hemachithra C, Meena N, Ramanathan R, et al. Immediate effect of horse riding simulator on adductor spasticity in children with cerebral palsy: a randomized controlled trial. Physiother Res Int 2020;25(1):e1809. DOI: 10.1002/pri.1809.
20. Pitcher CA, Elliott CM, Valentine JP, et al. Muscle morphology of the lower leg in ambulant children with spastic cerebral palsy. Muscle Nerve 2018;58(6):818–823. DOI: 10.1002/mus.26293.
21. Karamitopoulos MS, Nirenstein L. Neuromuscular foot: spastic erebral palsy. Foot Ankle Clin 2015;20(4):657–668. DOI: 10.1016/j.fcl.2015.07.008.
22. Brunner R. Principles of treatment of spastic palsy in children: a critical review. Orthopade 2014;43(7):643–648. DOI: 10.1007/s00132-013-2218-6.
23. Jiang H, Li X, Jin C, et al. Early diagnosis of spastic cerebral palsy in infants with periventricular white matter injury using diffusion tensor imaging. AJNR Am J Neuroradiol 2019;40(1):162–168. DOI: 10.3174/ajnr.A5914.
24. Kaandorp JJ, Benders MJ, Rademaker CM, et al. Antenatal allopurinol for reduction of birth asphyxia induced brain damage (ALLO-Trial); a randomized double blind placebo controlled multicenter study. BMC Pregnancy Childbirth 2010;10(1):1–6. DOI: 10.1186/1471-2393-10-8.
25. Remijn L, van den Engel-Hoek L, Satink T, et al. "Everyone sees you sitting there struggling with your food": experiences of adolescents and young adults with cerebral palsy. Disabil Rehabil 2019;41(16):1898–1905. DOI: 10.1080/09638288.2018.1451923.
26. Mukhopadhyay R, Mahadevappa M, Lenka PK, et al. Correction of toe-walking gait in children with spastic cerebral palsy by using electrical stimulation therapy. Conf Proc IEEE Eng Med Biol Soc 2018. 3529–3532. DOI: 10.1109/EMBC.2018.8513043.
27. Vaz DV, Cotta Mancini M, Fonseca ST, et al. Muscle stiffness and strength and their relation to hand function in children with hemiplegic cerebral palsy. Dev Med Child Neurol 2006;48(9):728–733. DOI: 10.1017/S0012162206001563.
28. Hoare BJ, Wallen MA, Thorley MN, et al. Constraint-induced movement therapy in children with unilateral cerebral palsy. Cochrane Database Syst Rev 2019;4:CD004149. DOI: 10.1002/14651858.CD004149.pub3.
29. Huntsman R, Lemire E, Norton J, et al. The differential diagnosis of spastic diplegia. Arch Dis Child 2015;100(5):500–504. DOI: 10.1136/archdischild-2014-307443.
30. Givon U. Muscle weakness in cerebral palsy. Acta Orthop Traumatol Turc 2009;43(2):87–93. DOI: 10.3944/AOTT.2009.087.
31. Pauk J, Ihnatouski M, Daunoraviciene K, et al. Research of the spatial-temporal gait parameters and pressure characteristic in spastic diplegia children. Acta Bioeng Biomech 2016;18(2):121–129.
32. Ozkan Y. Child's quality of life and mother's burden in spastic cerebral palsy: a topographical classification perspective. J Int Med Res 2018;46(8):3131–3137. DOI: 10.1177/0300060518772758.
33. Gormley ME, Krach LE, Piccini L. Spasticity management in the child with spastic quadriplegia. Eur J Neuro 2001;5(s5):127–135. DOI: 10.1046/j.1468-1331.2001.00045.x.
34. Monbaliu E, Himmelmann K, Lin JP, et al. Clinical presentation and management of dyskinetic cerebral palsy. Lancet Neurol 2017;16(9):741–749. DOI: 10.1016/S1474-4422(17)30252-1.
35. Beckung E, Hagberg G. Correlation between ICIDH handicap code and gross motor function classification system in children with cerebral palsy. Dev Med Child Neurol 2000;42(10):669–673. DOI: 10.1017/s0012162200001237.
36. Platt MJ, Krageloh-Mann I, Cans C. Surveillance of cerebral palsy in Europe: reference and training manual. Med Educ 2009;43(5):495–496. DOI: 10.1111/j.1365-2923.2009.03351.x.
37. Monbaliu E, de Cock P, Ortibus E, et al. Clinical patterns of dystonia and choreoathetosis in participants with dyskinetic cerebral palsy. Dev Med Child Neurol 2016;58(2):138–144. DOI: 10.1111/dmcn.12846.
38. Cheney PD. Pathophysiology of the corticospinal system and basal ganglia in cerebral palsy. Ment Ret and Dev Disa Res Rev 1998;3:153–167.
39. Manto MU, Pandolfo M. The cerebellum and its disorders. Cambridge: Camb Univ Press; 2002. pp. 97–120.
40. McHale D, Jackson A, Campbell D, et al. A gene for ataxic cerebral palsy maps to chromosome 9p12-q12. Eur J Hum Genet 2000;8(4):267–272. DOI: 10.1038/sj.ejhg.5200445.
41. Ingram TTS. Congenital ataxic syndromes in cerebral palsy. Acta Paediatr Scand 1962;51(2):209–221. DOI: 10.1111/j.1651-2227.1962.tb06531.x.

42. Straub K, Obrzut JE. Effects of cerebral palsy on neurophsyological function. J Dev and Phy Dis 2009;21(2):153–167. DOI: 10.1007/s10882-009-9130-3.
43. Zhou XJ, Qiu HB, Xu H, et al. Risk factors related to infantile spastic cerebral palsy among 145 cases. Zhonghua Liu Xing Bing Xue Za Zhi 2013;34(4):389–392.
44. Krageloh-Mann I, Cans C. Cerebral palsy update. Brain and Dev 2009;31(7):537–544. DOI: 10.1016/j.braindev.2009.03.009.
45. Öztürk A, Demirci F, Yavuz T, et al. Antenatal and delivery risk factors and prevalence of cerebral palsy in Duzce (Turkey). Brain Dev 2007;29(1):39–42. DOI: 10.1016/j.braindev.2006.05.011.
46. Strijbis EMM, Oudman I, van Essen P, et al. Cerebral palsy and application of the international criteria for acute intrapartum hypoxia. Obstet Gynecol 2006;107(6):1357–1365. DOI: 10.1097/01.AOG.0000220544.21316.80.
47. Hankins GDV, Speer M. Defining the pathogenesis and pathophysiology of neonatal encephalopathy and cerebral palsy. Obstet Gynecol 2003;102(3):628–636. DOI: 10.1016/s0029-7844(03)00574-x.
48. MacLennan A. A template for defining a causal relation between acute intrapartum events and cerebral palsy: International consensus statement. BMJ 1999;319(7216):1054–1059. DOI: 10.1136/bmj.319.7216.1054.
49. Suvanand S, Kapoor SK, Reddaiah VF, et al. Risk factors for cerebral palsy. Indian J Pediatr 1997;64(5):677–685. DOI: 10.1007/BF02726124.
50. Palmer FB. Strategies for the early diagnosis of cerebral palsy. J Pediatr 2004;145(2 Suppl):S8–S11. DOI: 10.1016/j.jpeds.2004.05.016.
51. Wu YW, Day SM, Strauss DJ, et al. Prognosis for ambulation in cerebral palsy: a population-based study. Pediatrics 2004;114(5):1264–1271. DOI: 10.1542/peds.2004-0114.
52. Park N, Lee J, Sung KH, et al. Design and validation of automated femoral bone morphology measurements in cerebral palsy. J Digit Imaging 2014;27(2):262–269. DOI: 10.1007/s10278-013-9643-2.
53. Choi JY, Choi YS, Rha D, et al. The clinical outcomes of deep gray matter injury in children with cerebral palsy in relation with brain magnetic resonance imaging. Res Dev Disabil 2016;55:218–225. DOI: 10.1016/j.ridd.2016.04.010.
54. Padfield N, Zabalza J, Zhao H, et al. EEG-based brain-computer Interfaces using motor-imagery: techniques and challenges. Sensors (Basel) 2019;19:1423.
55. Lee RW, Poretti A, Cohen JS, et al. A diagnostic approach for cerebral palsy in the genomic era. Neuromolecular Med 2014;16(4):821–844. DOI: 10.1007/s12017-014-8331-9.
56. O'Shea TM. Diagnosis, treatment, and prevention of cerebral palsy. Clin Obstet Gynecol 2000;51(4):816–828. DOI: 10.1097/GRF.0b013e3181870ba7.
57. O'Shea TM. Diagnosis, treatment, and prevention of cerebral palsy. Clin Obstet Gynecol 2008;51(4):816–828. DOI: 10.1097/GRF.0b013e3181870ba7.
58. Ji H, Tan S, Igarashi J, et al. Selective neuronal nitric oxide synthase inhibitors and the prevention of cerebral palsy. Ann Neurol 2009;65(2):209–217. DOI: 10.1002/ana.21555.
59. Lekic T, Manaenko A, Rolland W, et al. Neuroprotection by melatonin after germinal matrix hemorrhage in neonatal rats. Acta Neurochir Suppl 2011;111:201–206. DOI: 10.1007/978-3-7091-0693-8_34.
60. Lekic T, Manaenko A, Rolland W, et al. Protective effect of hydrogen gas therapy after germinal matrix hemorrhage in neonatal rats. Acta Neurochir Suppl 2011;111:237–241. DOI: 10.1007/978-3-7091-0693-8_40.
61. Conde-Agudelo A, Romero R. Antenatal magnesium sulfate for the prevention of cerebral palsy in preterm infants <34 weeks' gestation: a systematic review and metaanalysis. Am J Obstet Gynecol 2009;200(6):595–609. DOI: 10.1016/j.ajog.2009.04.005.
62. Haynes RL, Baud O, Li J, et al. Oxidative and nitrative injury in periventricular leukomalacia: a review. Brain Pathol 2005;15(3):225–233. DOI: 10.1111/j.1750-3639.2005.tb00525.x.
63. Gressens P, Schwendimann L, Husson I, et al. Agomelatine, a melatonin receptor agonist with 5-HT(2C) receptor antagonist properties, protects the developing murine white matter against excitotoxicity. Eur J Pharmacol 2008;588(1):58–63. DOI: 10.1016/j.ejphar.2008.04.016.
64. Girard S, Sébire H, Brochu ME, et al. Postnatal administration of IL-1Ra exerts neuroprotective effects following perinatal inflammation and/or hypoxic-ischemic injuries. Brain Behav Immun 2012;26(8):1331–1339. DOI: 10.1016/j.bbi.2012.09.001.
65. Wei X, Du Z, Zhao L, et al. IFATS collection: The conditioned media of adipose stromal cells protect against hypoxia-ischemia-induced brain damage in neonatal rats. Stem Cells 2009;27(2):478–488. DOI: 10.1634/stemcells.2008-0333.
66. Fantacci C, Capozzi D, Ferrara P, et al. Neuroprotective role of nerve growth factor in hypoxic-ischemic brain injury. Brain Sci 2013;3(4):1013–1022. DOI: 10.3390/brainsci3031013.
67. Harvey AR, Baker LB, Reddihough DS, et al. Trihexyphenidyl for dystonia in cerebral palsy. Syst Rev 2018;5:CD012430. DOI: 10.1002/14651858.CD012430.pub2.
68. Li Q, Li H, Roughton K, et al. Lithium reduces apoptosis and autophagy after neonatal hypoxia–ischemia. Cell Death Dis 2010;1(7):e56. DOI: 10.1038/cddis.2010.33.
69. Koldoff EA, Holtzclaw BJ. Physical activity among adolescents with cerebral palsy: an integrative review. J Pediatr Nurs 2015;30(5):e105–117. DOI: 10.1016/j.pedn.2015.05.027.
70. Dias BLS, Fernandes AR, Filho MHS. Treatment of drooling with sublingual atropine sulfate in children and adolescents with cerebral palsy. Arq Neuropsiquiatr 2017;75(5):282–287. DOI: 10.1590/0004-282x20170033.
71. Garcia SSF, Gomez GMT, Guzman PJE. Toxina botulinica A y terapia fisica, en la marcha en parilisis cerebral botulinum toxin A and physical therapy in gait in cerebral palsy. Rev Med Inst Mex Seguro Soc 2017;55:18–24.
72. Gonnade N, Lokhande V, Ajij M, et al. Phenol versus botulinum toxin a injection in ambulatory cerebral palsy spastic diplegia: a comparative study. J Pediatr Neurosci 2017;12(4):338–343. DOI: 10.4103/jpn.JPN_123_17.
73. Hsieh YL, Yang CC, Sun SH, et al. Effects of hippotherapy on body functions, activities and participation in children with cerebral palsy based on ICF-CY assessments. Disabil Rehabil 2017;39(17):1703–1713. DOI: 10.1080/09638288.2016.1207108.
74. Tekin F, Kavlak E, Cavlak U, et al. Effectiveness of neuro-developmental treatment (bobath concept) on postural control and balance in cerebral palsied children. J Back Musculoskelet Rehabil 2018;31(2):397–403. DOI: 10.3233/BMR-170813.
75. Aboutorabi A, Arazpour M, Ahmadi Bani M, et al. Efficacy of ankle foot orthoses types on walking in children with cerebral palsy: a systematic review. Ann Phys Rehabil Med 2017;60(6):393–402. DOI: 10.1016/j.rehab.2017.05.004.