International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

An comprehensive review and update of current concepts in cerebral palsy

Laghane P.M, Vyas G.V, Wankhede S.S
[1,2,3] *Assistant professor in ' Institute of pharmacy Badnapur*
Corresponding Author Vyas G V

Submitted: 17-12-2022 Accepted: 28-12-2022

ABSTRACT: Although spastic paralysis could be a clinical identification, trendy diagnostic imaging provides data that enables the division of the results of resonance imaging in youngsters with spastic paralysis into 5 teams in step with the resonance imaging arrangement. even as the clinical presentation and also the factors predisposing for CP area unit terribly numerous, treatment is additionally a awfully complicated drawback. trendy treatment of fitfulness includes each neurolysin therapies and surgical techniques, eg, rhizotomy. These article gift current views on definitions, risk factors, medicine and treatment of CP in addition as comorbid issues, eg, drug-resistant brain disorder. spastic paralysis (CP) could be a common medicine disorder occurring in concerning two to two.5 per one thousand live births. it's a chronic motor disorder ensuing from a non-progressive (static) insult to the developing brain. CP is that the clinical presentation of a good form of cerebral plant tissue or sub-cortical insults occurring throughout the primary year of life. the most typical explanation for CP remains unknown in five hundredth of the cases; immatureness remains the most typical risk factorThe risk factors for CP will be divided into preconception, prenatal, perinatal and postpartum ones. CP ordinarily co-exists with brain disorder, above all drug-resistant brain disorder, however additionally with retardation, visual and handicap, in addition as feeding and activity disorders. The degree of motor drawback varies from delicate to terribly severe creating the kid entirely obsessed on caregivers. spastic paralysis is split into forms reckoning on the sort of motor disorders that dominate the clinical presentation; youngsters with CP suffer from multiple issues and potential disabilities like retardation, epilepsy, feeding difficulties, and ophthalmologic and hearing impairments. Screening for these conditions ought to be a part of the initial assessment.Management of fitfulness will be difficult with a good form of doable therapeutic interventions. The treatment should be goal orientating, like to help with quality, scale back or stop contractures, improve positioning and hygiene, and supply comfort. every member of the child's multidisciplinary team, together with the kid and each oldsters, ought to participate within the serial evaluations and treatment designing. medicament medication, mortise joint casting, neurolysin for focal fitfulness, bisphosphonates, diazepam, hip police work, and dorsal surgical procedure area unit effective. Therapies like hyperbaric element, hip bracing, and neurodevelopmental medical aid once kid contractures area unit already developed area unit ineffective. within the last decade, the proof on CP has apace enlarged, providing clinicians and families with the chance of newer, safer, and more practical interventions. during this update, the author reviews this proof of the management of CP and provides a comprehensive analysis and multidisciplinary management..

KEYWORDS: Cerebral palsy, Birth asphyxia, Hypoxic-ischemic encephalopathy, Early intervention, Multidisciplinary management, Early intervention requires early identification, Of infants with possible cerebral palsy

I. INTRODUCTION

Cerebral palsy (CP) isn't an outlined, separate sickness classification, however AN umbrella term encompassing aetiologically numerous symptoms, that amendment with age[1]. The term "cerebral paralysis" was used for the primary time over a hundred and seventy years agone, by English people orthopedical physician William very little, United Nations agency correlative a troublesome labour and babe drive with limb fitfulness and eventful contractor deformities.1 Over the years, the definition of spastic paralysis has been repeatedly modified.2–4 per the present definition, developed by a world team of consultants, spastic paralysis may be a cluster of permanent, however not unchanging, [2,3]disorders of

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

movement and/or posture and of motor operate, that ar because of a non-progressive interference, lesion, or abnormality of the developing/ immature brain.The identification of spastic paralysis is especially supported motor operate and posture disorders that occur in babyhood and persist till the tip of life; they're non-progressive, however amendment with age.[4,5] Motor operate disorders, that ar the core symptoms of spastic paralysis, ar oftentimes in the course of alternative dysfunctions, such as: sensation, perceptual, cognitive, communication and behavioral disorders, epilepsy, and secondary contractor disorders. several metabolic and non-progressive genetic disorders might gift with motor disfunction resembling spastic paralysis. Such disorders ar usually characterised as CP mimics.[6,7] There ar reports within the literature of inborn errors of metabolism that gift as CP mimics; an oversized proportion of those diseases ar treatable specified medicine injury will either be reversed or prevented.9 the first aetiology of a spastic paralysis syndrome must always be known if doable. this is often significantly necessary within the case of genetic or metabolic disorders that have specific disease-modifying treatment.[8] creating a certain identification of a metabolic or genetic disease has necessary implications for the likelihood of treatment, correct prognosis and genetic direction. The aim of the current literature review was to debate current views on definitions, risk factors, medicine and treatment of CP furthermore as comorbid issues, eg, drug-resistant brain disease.Mechanism.

EPIDEMIOLOGY

The worldwide incidence of CP is just about two to two.5/1000 live births. The incidence is powerfully related to fertilization age, occurring in one of twenty living preterm infants.[9] it's vital to notice that though immaturity is that the commonest risk issue for developing CP, the bulk of affected kids square measure full-term . this could be explained by the actual fact that there square measure more full-term than preterm infants born at a given time.3 Despite the reduction within the rate of birth physiological state from 40/100 000 in 1979 to 11/100 000 in 1996[10], no associated reduction within the prevalence or incidence of CP was seen.4 In fact, the prevalence of CP within the USA multiplied by 2 hundredth (from one.9 to 2.3/1000 live births) between 1960 and 1986.[11] This increase is probably going associated with the survival of terribly low birth weight premature infants.5 there's additionally proof of associate associated increase within the severity of the incapacity[12]. This emphasizes the requirement for a lot of efforts to decrease the speed of immaturity additionally to decreasing the associated medical specialty injury among these infants.

FREQUENCY OF CEREBRAL PALSY INCIDENCE

The average incidence of spastic paralysis is calculable to vary between one.5 and 3.0 per a thousand live births; these values modification among elite teams of patients, reckoning on numerous risk factors.8 an enormous role within the compilation of medical specialty information regarding a number[13] of the ecu countries was compete by police work of spastic paralysis in Europe (SCPE), containing registers of sick kids from completely different European centres, that was established in 1998 victimization funds from the ecu Commission. SCPE was created thanks to the need of standardizing and harmonizing the definitions of spastic paralysis additionally because[14] the inclusion and exclusion criteria, in order that researchers and practitioners handling spastic paralysis might use a "common" language[15]. The activity of SCPE was aimed toward making a standardized info, initiating cooperation in analysis comes, gaining a stronger understanding of CP causes and rising the standards of look after kids with spastic paralysis.7 initio, SCPE was composed of fourteen centres in eight European countries; within the following years, it absolutely was augmented to incorporate extra centres.7 presently SCPE has twenty five active centres in twenty European countries[18]:Oesterreich, Belgium, Croatia, Denmark, France, Greece, Spain, Ireland, Iceland, Latvia, Malta, Germany, Norway, Portugal, Slovenia, Svizzera, Sweden, Hungary, the uk and European country. SCPE work is administered by specialists handling CP problems in numerous fields, ie, epidemiologists, pediatric neurologists, neonatologists,paediatricians,gynaecologists,[19] geneticists, surgeons, orthopaedists, public health specialists, physiotherapists, activity therapists, speech and language therapists, nutritionists and social staff. SCPE work has contributed to the analysis of CP incidence at completely different time intervals, above all reckoning on the birth weight.13,14 information from the register of 6500 kids with CP from thirteen European centres, that were revealed in 2002 and anxious the years 1980–1990, allowed for estimating the common incidence of CP as two.08 per a thousand live births; but, the incidence among premature babies with birth weight below 1500 grams was quite seventy times on top of in kids with birth weight of 2500 grams and a lot

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

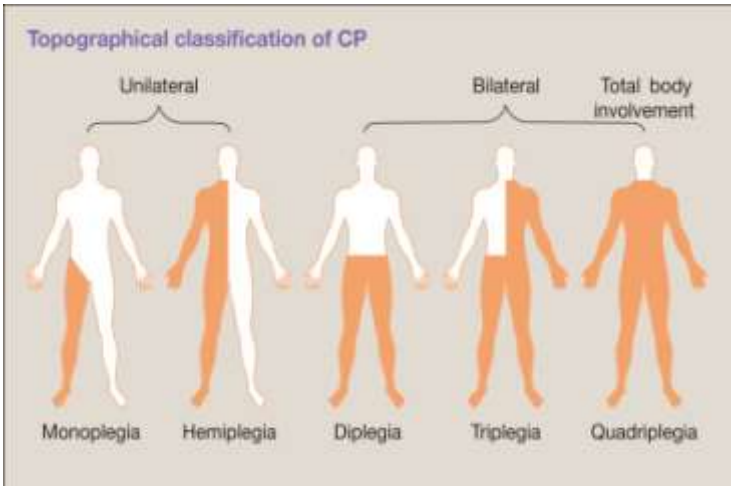
of.13 Another study involved the analysis of CP incidence in infants born within the years 1980–1996 with birth weight below 1500 g in sixteen European countries. CP incidence during this cluster of kids diminished from sixty.6 per a thousand live births in 1980 to thirty-nine.5 per a thousand live births in 1996.14 elaborated information on CP incidence reckoning on a baby's maturity at birth was provided by the meta-analysis of analysis results revealed within the years 1985–2006, conducted by Belgian researchers[20].15 The results were compared for four groups: premature infants born before the twenty eighth week of maternity, those born between the 28th-31st week of maternity, those born between the 32nd-36th week of maternity, and babies born later than the thirty seventh week of maternity[21]. The incidence of CP ranged from one46 cases per a thousand live births within the initial cluster of kids to 1.13 cases per a thousand live births within the cluster of kids born when the thirty seventh week of maternity. within the remaining 2 teams, these indicators reached 62/1000 (for kids born between the 28th-31st week of pregnancy) and 7/ a thousand (for infants born between the 32nd-36th week of pregnancy), severally. In 2013, Canadian researchers, Oskoui et al, conducted a meta-analysis of CP incidence supported an issue literature review from the years 1990–2005, taking into thought each the birth weight and vertebrate age of infants.16 the final incidence of CP was established as two.11/1000 live births; the best indicator was noted for babies whose birth weight ranged from a thousand g to 1499 g (59.18/1000 live births) and for babies born before the twenty eighth week of maternity (111.8/1000 live births). The multi-centre study supported SCPE registers, revealed in 2016, that involved the years 1980–2003[22], showed a downward trend in CP incidence.17 the final incidence of spastic paralysis born from one.90/1000 live births in one980 to 1.77/1000 live births in 2003. The downward trend was additionally noted within the case of babies with a really low birth weight (VLBW), ie, 1000–1499 g (a decrease from seventy.9/1000 to thirty five.9/1000), and babies with a coffee birth weight (LBW), ie, 1500–2499 g (a decrease from eight.5/1000 to six.2/1000). in step with the authors, in kids with birth weight over 2499 g, a statistically insignificant downward trend (from one.17 to 0.89/1000) may be determined[23]. The incidence of CP in babies with an especially low birth weight (ELBW), ie, below a thousand g, was at a stable level – a mean of forty two.4/1000 live births. throughout that point, however, the rates of each birth and survival of premature babies with ELBW clearly augmented thanks to respectable advances in tocology (modern strategies of antenatal medical specialty, in-utero transport, intensive baby care).17

TYPE AND CLASSIFICATION OF CEREBRAL PALSY

Clinical manifestations and classification schemes youngsters with CP typically gift with organic process delay and motor deficits. the excellence between a static (non-progressive) and progressive clinical course is incredibly vital. Classically, loss of antecedently nonheritable milestones (regression) marks the onset of most metabolic and neurodegenerative disorders (NDD). However, some NDD or metabolic disorders have a slow rate of progression and might be misdiagnosed as CP. so, clear organic process regression might not be evident, notably within the early stages of the sickness or at a younger age of onset. additionally, the medical specialty consequences of CP is also delayed for many months thanks to the state of the systema nervosum[24].Motor deficits of CP embrace negative phenomena like weakness, fatigue, unskillfulness and positive phenomena like fitfulness, clonus, rigidity, and spasms. fitfulness could be a speed dependent accrued tonicity with hyperreflexia ensuing from hyperexcitability of the myotactic reflex. It will result in muscle stiffness, purposeful impairment, and atrophy. If not treated, it will achieve muscle pathology, contractures, and resultant contractor deformities.[25] CP are often classified in keeping with the severity of motor deficits as delicate, moderate, or severe. many different classification systems exist supported the pathophysiology, etiology, and distribution of motor deficits as follows. Pathophysiologic classification Insults leading to neuronic loss are often 1) plant tissue (pyramidal), leading to fitfulness, 2) basal ganglial (extrapyramidal), leading to abnormal movements like choreoathetosis, 3) neural structure, leading to hypotonus, or 4) mixed. Spastic CP is that the most typical sort, accounting for up to seventy fifth of cases.8A smaller proportion of kids with CP demonstrate extrapyramidal (dyskinetic) options, together with combos of nervous disorder, chorea, and dystonia. The abnormal movements typically develop within the second year of life and become most apparent throughout willing motor activities with associated speech impairments. most kids with extrapyramidal[26] CP have traditional intelligence, however their skills are often underestimated because of the severity of their motor and communication deficits. icterus (bilirubin encephalopathy) could be a leading reason for extrapyramidal CP. The affected newborn infant

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

seems weak, listless, and hypotonic, with poor feeding. Over a amount of months, hypertonia, opisthotonus, choreoathetosis, and sensorineural deafness develops. Hypotonic encephalopathy happens rarely; but, most kids achieve different CP subtypes. Mixed CP happens once the kid displays a mixture of options, like fitfulness and choreoathetosis. Etiologic Classification Up to five hundredth of CP cases haven't any acknowledgeable underlying etiology. The etiologies are often classified according the temporal arrangement of the insult as antepartum (commonest), natal, or postpartum. Another etiologic arrangement depends on the particular cause like innate (developmental, malformations, syndromic) or nonheritable (traumatic, infectious, hypoxic, ischemic, TORCH infections, and others). perinatal physiological condition could be a cause in just V-day to fifteen of all cases.9 Most of those youngsters have clinical options of baby hypoxic anemia brain disorder (HIE) like a disturbed level of consciousness, seizures, and different organ disfunction. though a traditional twine hydrogen ion concentration excludes Classification of Motor disfunction CP are often classified in keeping with the topographical distribution of motor involvement. Motor deficits embrace palsy, diplegia, hemiplegia, triplegia,quadriplegia, and double paralysis. paralysis is gift once the lower extremities area unit primarily affected, though the higher extremities aren't fully spared. Spastic paralysis is that the most typical sort of CP and is related to immaturity. The periventricular germinal matrix, that could be a region of active neuronic proliferation, is especially prone to hemorrhage and hypoxic anemia injury. the encircling periventricular nerve tissue contains pyramidic fibers that descend through the inner capsule to provide the lower limbs. additional peripheral within the periventricular nerve tissue area unit the pyramidic tracts of the higher limbs. Therefore, periventricular insult in preterm infants affects the lower limbs quite the higher limbs, leading to spastic paralysis. Note that the term paralysis shouldn't be utilized in this context because it implies a neural structure insult leading to lower motor nerve fiber lesion involving the lower limbs solely, i.e. not cerebral in origin with fully traditional arm perform. paralysis is characterised by involvement of 1 facet of the body, with the arm generally additional affected than the leg. this can be thanks to larger plant tissue illustration (motor homunculus) of the hand and arm compared to a smaller leg space. palsy refers to single limb involvement. this can be typically the results of terribly delicate paralysis with arm deficits solely. once all four limbs area unit concerned, palsy is that the acceptable descriptive term. this can be the foremost disabling, with twenty fifth of the affected youngsters requiring total care.1 Double paralysis refers to the kid with palsy involving the arms quite the legs with facet imbalance. Triplegia is rare and typically results from milder and extremely uneven double paralysis (sparing one leg) or milder uneven paralysis (sparing one arm). These subtypes are often tough to delineate clinically in some youngsters, notably since the degrees of incapacity will vary wide at intervals these subtypes.



International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

EVALUATION

Comprehension analysis of youngsters with CP

The comprehensive analysis and care of a toddler with CP will be simplified into the subsequent 5 steps: Confirming the diagnosing and determinative the cause, grouping "the team," assessing purposeful skills, determinative goals of care, and comprehensive care initiation[44]

Step 1: Confirming the diagnosing and determinative the cause This step includes an in depth history taking and examination followed by necessary investigations like computed axial tomography (CT) or resonance imaging (MRI) of brain and supportive investigations like electroencephalography (EEG), metabolic, genetic, and coagulopathy testing. yank Academy of Neurology (AAN) recommendations on neuroimaging: Neuroimaging is suggested within the analysis of a toddler with CP if the etiology has not been established[45,46]. imaging is healthier than CT scanning because the yield of imaging is higher and helps within the identification of temporal order of insult (Level A, category I-III evidence).

Step 2: grouping the team this can embrace a coordinated approach between varied branches of drugs in providing complete care to a toddler with CP.

Step 3: the entire assessment This step includes a comprehensive and in depth analysis of the purposeful skills, comorbidities, and therefore the network of youngsters with CP. It will be additional divided into the subsequent steps: one. quality and motor impairment analysis two. Associative conditions assessment three. Activities of daily living analysis four. Family dynamics and socioeconomic standing assessment five. instructional assessment

B. Associative conditions assessment: AAN recommendation on further testing for comorbidities: because of the high incidence of associated conditions, youngsters with CP ought to be screened for "intellectual incapacity, ophthalmologic and hearing impairments, and speech and language disorders" (Level A, category I and II evidence)[47,48,49]. observation ought to be in dire straits nutrition, growth, and swallowing pathology. If screening tests square measure suggestive impairments, it ought to be confirmed by different diagnostic tests

. C. Activities of daily living evaluation: the subsequent points square measure to be noted to grant acceptable help as per the impairment, bathing, dressing and undressing, eating, food preparation, grooming, work, leisure, and play; recreation, personal hygiene, mobility, self-care, shopping, transferring (bed, chair, toiletry, etc.), and work

Step 5: Coordinated, comprehensive care arrange implementation once an in depth analysis, multidisciplinary care is enforced with the assistance of the team gathered therefore on reach the goals set. Ashwal et al. have provided a observe parameter for diagnostic assessment and analysis of a toddler with CP[47,48,49], that provides a comprehensive flow chart for analysis.

Muscle tone: Modified Ashworth Scale is used for tone assessment, as shown in [Table 1].

Table 6: Modified Ashworth scoring system.

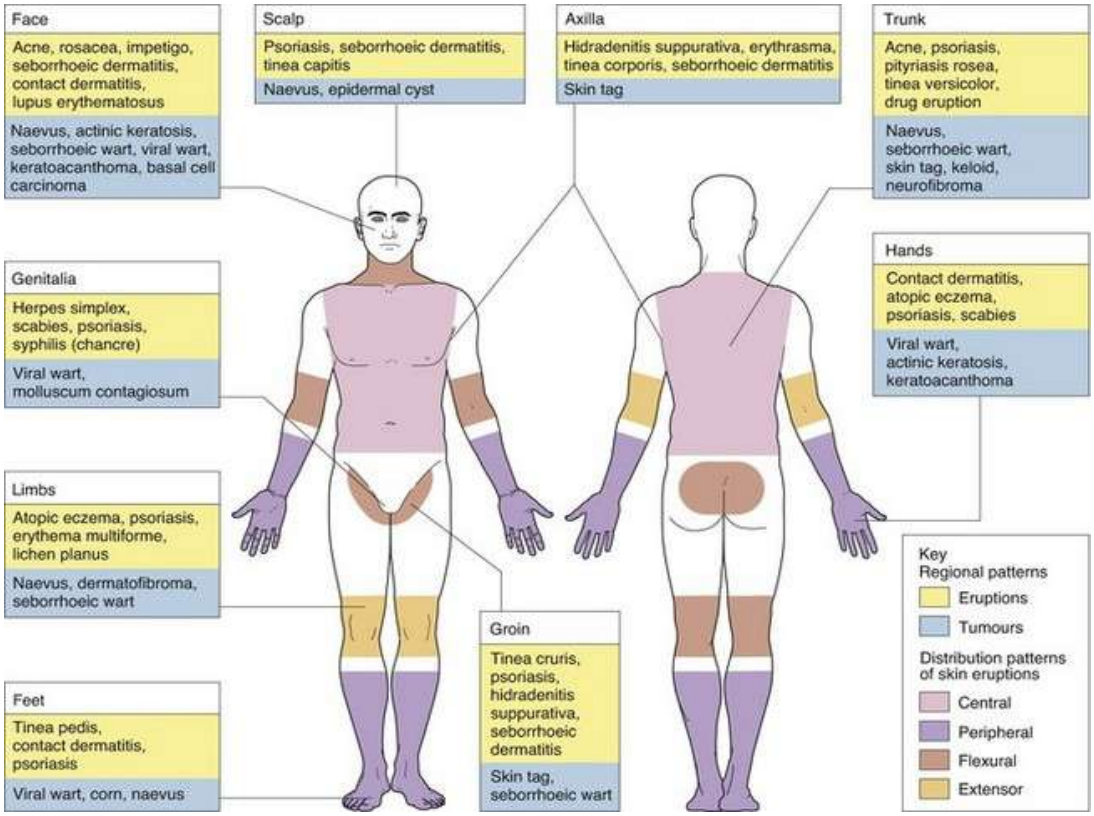
Grade 0	No increase in muscle tone
Grade 1	Grade 1 Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
Grade 1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
Grade 3	More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

Grade 3	Considerable increase in muscle tone, passive movement difficult
Grade 4	Affected part(s) rigid in flexion or extension

DIAGNOSTIC PROCEDURE IN CEREBRAL PALSY

Cerebral Palsy medicine Procedures designation of brain disorder relies on clinical presentation, a particular interview regarding the physiological state, labour, baby and child amount, the course of development and also the currentperformance of the child's motor functions. extra examinations will facilitate in CP designation[46]. Neuroimaging Examination vital info is provided by neuroimaging examination, ie, brain ultrasound in infants, pc pictorial representation in older youngsters, and particularly, resonance imaging (MRI) of the brain. magnetic resonance imaging are often conducted for foetuses and untimely born babies. The results of imaging studies straight forward interpretation and classification of brain MRI results by each clinicians and alternative victimisation the magnetic resonance imaging technique demonstrate abnormalities in additional than eightieth of patients with CP[47,48]. magnetic resonance imaging examination reveals anatomic anomalies characteristic of specific CP types; it additionally permits for an improved understanding of pathologic process, brain injury aetiology and structuralfunctional dependencies in CP. Work conducted by SCPE has junction rectifier to the institution of a system of magnetic resonance imaging results classification (magnetic resonance imaging organisation, MRICS) for youngsters with brain disorder[49,50,51]. Recommendations for this organisation were revealed on-line in 2016, so written in 2017. The aim of the magnetic resonance imagingCS is to change specialists managing CP patients. consistent with MRICS,



International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

Table 2 Classification into a particular level of performance according to data from the Gross Motor Function Classification System (GMFCS) [52]

Level of Performance	Characteristics
I	The patient can walk freely
II	The patient walks on their own with certain (slight) limitations
III	The patient walks using ancillary equipment
IV	The patient can move on their own but with certain limitations; he/she can use an electric wheelchair
V	The patient is not able to move on their own; he/ she is transported in a wheelchair by a carer

images in youngsters with CP ar classified into 5 main groups:
A. Maldevelopments;
B. Predominant nerve tissue injury;
C. Predominant grey substance injury;
D. Miscellaneous;
E. Normal.30 consistent with SCPE recommendations, if there ar many patterns, the predominant pattern that's believed to be presumably to possess junction rectifier to the CP ought to be classified first; if there's another unhealthful pattern (A, B or C), this could be classified individually. thanks to the myelination method development within the initial years of life[23,54], SCPE recommends classifying adult male pictures performed when the kid has reached a pair of years ancient consistent with the MRICS system, unless the previous pictures unconcealed a selected pathology.Figure a pair of presents chosen samples of resonance imaging from the authors' own analysis. typical adult male imaging has limitations in delineating nerve tissue tracts exactly[55,56]. a strong technique providing precise identification of nerve tissue microstructure is diffusion tensor imaging (DTI). Diffusion tensor imaging captures restrictions within the random movement of water protons by macromolecules and medulla to check brain nerve tissue tracts. It are often wont to produce two- and three-dimensional color maps of traditional nerve tissue design and to produce a lot of precise identification of nerve tissue infertility and injury than typical imaging. DTI is exclusive in its ability to non-invasively visualize nerve tissue fibre tracts within the human brain. it's effective in up diagnostic accuracy and provides new info concerning the character and extent of patterns of nerve tissue cerebral abnormalities in youngsters with CP. It shows varied nerve tissue injury patterns in patients with PVL, with the foremost frequent injuries being to the retrolenticular a part of the interior capsule, posterior thalamic radiation, superior corona radiata and commissural fibres. This technique indicates that nerve tissue tracts from each the modality and cortical region play a vital role within the pathophysiology of motor incapacity in CP patients[54,55,56]DTI metrics (lower half property and better crosswise diffusivity) within the down pointed tracts correlate with a lot of important motor impairment. DTI imaging additionally shows that the motor dysfunctions in periventricular leukomalacia could, in part, mirror disruption of sensory connections outside the classic pointed motor pathways. A meta-analysis of DTI studies revealed from January 1999 to January 2019 shows that half property (DTI metric) inside the posterior a part of the interior capsule is a lot of closely associated with motor dysfunctions and may probably be a biomarker for evaluating the degree of motor impairment in spastic brain disorder[54,55,56] the opposite neuroimaging modalities which may be employed in CP patients are: magnetoencephalography (MEG), practical magnetic resonance imaging (fMRI), and volumetrical magnetic resonance imaging of gray and nerve tissue. There are multimodal studies that mix findings from totally different neuroimaging strategies. The results of those studies may facilitate in understanding the practical and structural changes in brain disorder. Other extra Examinations Due to the complexness of issues within the clinical presentation of CP, psychological tests, vision analysis, measuring tests and

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

electroencephalography (EEG) are administrated.7 the worth of graphical record, particularly video graphical record, can't be overestimated within the differentiation of each non-epileptic attack disorders, [57,58]as well as involuntary movements, and kinds of epileptic seizures in youngsters affected by CP and co-existing encephalopathy Age of brain disorder designation CP designation isn't straightforward – it should be preceded by an in depth interview, AN analysis of the course of the child's development and also the results of extra tests. It additionally needs a comparatively long clinical observation amount. To diagnose brain disorder, one has to distinguish it from alternative motor disorders, with a unique nature and course. Some neuro developmental disorders in formative years are often temporary, whereas progressive motor disorders, a minimum of within the period of play of unwellness, will have an identical clinical presentation to it of CP[56,57,58] Taking into thought the central systema nervosum maturation, brain physical property and also the dynamic clinical presentation, the ultimate identification of CP, especially of a number of its varieties, can not be created prior at many years recent. However, typically the symptoms indicating the likelihood of CP ar gift already in early infancy. In such cases, delayed identification will result in a delay in enterprise correct treatment, and, in consequence, to the more serious functioning of the kid and his/her family within the future[56,57,58]. There ar varied studies that examine diagnostic tools enabling Associate in Nursing early identification, particularly in newborn babies happiness to the unsound cluster, ie, premature patients, with an occasional birth weight or abnormalities in neuroimaging. In consequence, Associate in Nursing early identification permits for early implementation of medical interventions thus on optimize the motor and psychological feature functions thanks to brain malleability, stop secondary lesions, and improve the standard of the child's life, however additionally his/her well-being and also the quality of lifetime of his/her carers. crucial the precise age at that the ultimate identification of spastic paralysis ought to be created is Associate in Nursing equivocal issue. For the requirements of international analysis programmes, supported registers of patients with CP in several components of the planet, like the New South Wales CP Register, the Western Australian CP Register and SCPE, it absolutely was necessary to ascertain common criteria for CP identification, and inclusion/exclusion criteria, together with the criterion old-time. The reciprocally in agreement criterion old-time permits for collection all the info and confirming the identification.[56,57,58] within the majority of registering programmes, this age was established as five years. the ultimate recommendation, however, is that the kid ought to have reached four years old-time so as to be properly diagnosed with CP. alternative Medical issues Co-Existing with Motor incapacity in CP Patients brain disorder in kids with spastic paralysis brain disorder could be a separate, vital clinical downside in kids with CP. Its incidence ranges from fifteen to 55–60%, and in line with some authors, even up to 90–94% of youngsters and adults with CP.45–49 brain disorder in kids with CP is usually disclosed within the 1st 4–5 years of life, sometimes within the 1st year of life The incidence of brain disorder varies betting on the kind of spastic paralysis. brain disorder is sometimes discovered in tetraplegia (50–94%); it oft accompanies unilateral paralysis (33–- 50%), however it rarely affects kids stricken by palsy and also the atactic sort of CP (16–27%).There ar several studies regarding risk factors for brain disorder in kids with CP. one in all the numerous factors is subnormality.[56,57,58] it's calculable that over five hundredth of youngsters with CP and subnormality suffer from brain disorder. The results of investigations additionally indicate a correlation between infant convulsions and a better risk of brain disorder in kids with CP. loads of knowledge on the incidence of brain disorder, also because the correlation between brain disorder and also the course of the time of life, incidental disorders and also the sort of CP was provided by population studies conducted by Sellier et al. They were supported SCPE registers from seventeen regions and anxious kids with CP born within the years 1976–1998. This analysis disclosed a general trend for Associate in Nursing exaggerated incidence of brain disorder among kids with CP within the years 1976–1983, followed by a come by the years 1983–1998. brain disorder sometimes occurred in kids with the dyskinetic and bilaterally spastic sort of CP and in kids with incidental vision and hearing disorders, subnormality and also the inability to run. within the case of those kids, brain disorder risk factors were brain development malformations, day of the month birth or moderately preterm birth (compared to terribly preterm birth), infant convulsions, artificial metabolism support, also as treatment in Associate in Nursing medical care Unit.53 Co-existence of brain disorder in an exceedingly kid with CP will increase the chance of death, together with questionable fast sudden death in brain disorder (SUDEP). this idea is known because the fast, sudden death of someone stricken by brain disorder (in the presence of witnesses or

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

while not them), that isn't associated with Associate in Nursing injury or drowning. Death happens in "mild circumstances"; it should occur throughout a seizure or while not one, [56,57,58]however not in epilepsy. Autopsy doesn't reveal the explanation for death. the chance of SUDEP is that the highest among young adults (aged 20–45) stricken by brain disorder. within the population of youngsters, the chance of SUDEP is ten times lower – it's calculable to succeed in one.1–3.4/ one thousand unwell kids annually. the foremost risk issue for SUDEP is that the high frequency of generalized tonic-clonic seizures also because the presence of night seizures. alternative risk factors embrace the first onset of brain disorder, male sex, subnormality, long period of unhealthiness, polytherapy, and prone position throughout sleep. subnormality Intellectual incapacity is a vital and comparatively common incidental impairment in CP that has the potential to more have an effect on daily activities, burden of care, quality of life, effectiveness of interventions, and longevity.[56,57,58] Intellectual organic process incapacity is outlined by important delay in 2 or a lot of organic process domains at less than five years recent, Associate in Nursingd Associate in Nursing I.Q. of seventy and below at an older age.9 The proportion of youngsters with CP and intellectual impairment varies between four-hundredth and sixty fifth. The frequency of intellectual incapacity has been according to be comparatively higher in association with paralysis, poor gross motor operate, and brain disorder. there's additionally Associate in Nursing association between brain disorder in kids with spastic paralysis and also the degree of mental impairment. The incidence of brain disorder in CP, principally in kids with unilateral paralysis and palsy, is related to reduced mental capacities.61 deficiency disease and duct Complications the bulk of youngsters with spastic paralysis have feeding difficulties and duct issues like bodily cavity dysfunctions, passageway illness, and constipation. Oral feeding could be a advanced method requiring a mature intake ability Associate in Nursingd an particularly mature coordination of intake with respiratory and swallowing. kids with spastic paralysis usually have problem with intake. alimental intake could be a extremely organized method that's essential for infants' feeding throughout the primary vi months of their lives. Associate in Nursing infant's inability to perform a secure Associate in Nursingd productive oral feeding may be an early detector of state of the central system. A pilot study shows, mistreatment diffusion imaging, the link between alimental intake patterns and also the microstructural integrity of sensory-motor tracts in newborns with brain injury. Feeding difficulties among kids with CP play a vital role within the pathological process of deficiency disease and increase the chance of growth failure.Physical growth could be a amount of health and well-being in kids.66 Besides growth failure, the results of deficiency disease embrace ablated cerebral operate, impaired immune operate, impaired circulation with poor wound healing, and diminished metabolism muscle strength. bodily cavity disorder is discovered in a pair of out of three kids with CP and is thought to influence not solely their nutritionary standing, however additionally their metabolism health and parental stress. Researchers from Oxford in their study found that 2 hundredth of oldsters according feeding as trying or unenjoyable, with exaggerated rates of stress with increasing gross motor impairment severity. In spastic paralysis, growth and nutrition disorders ar common. they will be gift among all kids with CP; but, they're a lot of distinguished among those with increasing severity of motor impairments. Speech issues Over five hundredth of youngsters with CP exhibit some kind of speech impairment. speaking involves respiration beside vocal organ, velopharyngeal and articulative movements, and any of those functions is also hampered in CP. Motor disorders poignant speech embrace dysarthria/anarthria and dyspraxia/apraxia of speech. speech disorder is characterised by slow, weak, general and/or uncoordinated movements of the speech muscular structure. Apraxia/dyspraxia is characterised by a disturbance within the motor coming up with and programming of speech movements.Speech ability is expounded to the kind of CP, gross motor operate, the presence of subnormality and also the localization of brain maldevelopment and lesions.70 Associate in Nursing association between the kind of CP and speech ability was according by author et al within the Norwegian study. Ninety % of the kids with unilateral spastic CP had traditional or graspable speech, whereas ninety seven of the kids with dyskinetic CP had severely impaired or no speech.

MANAGEMENT

Medical management of CP

Wide assortments of medications are used in CP to reduce symptoms and address complications and treat comorbidities. Children who experience spasticity and unwanted or uncontrolled involuntary movements such as dystonia, chorea, and athetosis are often prescribed drugs to minimize the movements, relax muscles, increase comfort, and facilitate better posture and functionality. Drug

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

therapy is also used to treat seizures, behavioral issues, pain, bowel movements, and manage other comorbidities and improve quality of life.
Spasticity management [59,60]
Spasticity treatment may include one or more of the following options: 1. Oral medications 2. Chemical blockage: Botulinum toxin and/or phenol 3. Intrathecal baclofen pump 4. Surgical management 5. Physical measures such as physiotherapy, occupational therapy, orthosis, and plaster caster use

The most commonly used drugs and dosages are:
1. Baclofen – dose 0.12–1 mg/kg/day
2. Tizanidine – 0.3 mg–0.5 mg/kg/day
3. Benzodiazepines (e.g., diazepam – 0.12–0.8 mg/kg/day and clonazepam – 0.01–005 mg/kg/day)
4. Dantrolene sodium: 3–12 mg/kg/day.

FEW TIPS TO SELECT DRUGS FOR SPASTICITY
1. Intractable seizures AND seizure tendency – avoid baclofen
2. Spasticity AND dystonia – baclofen
3. Sleep problems – bedtime diazepam/tizanidine
4. Myoclonus – clonazepam
5. Liver problems – avoid tizanidine, dantrolene.

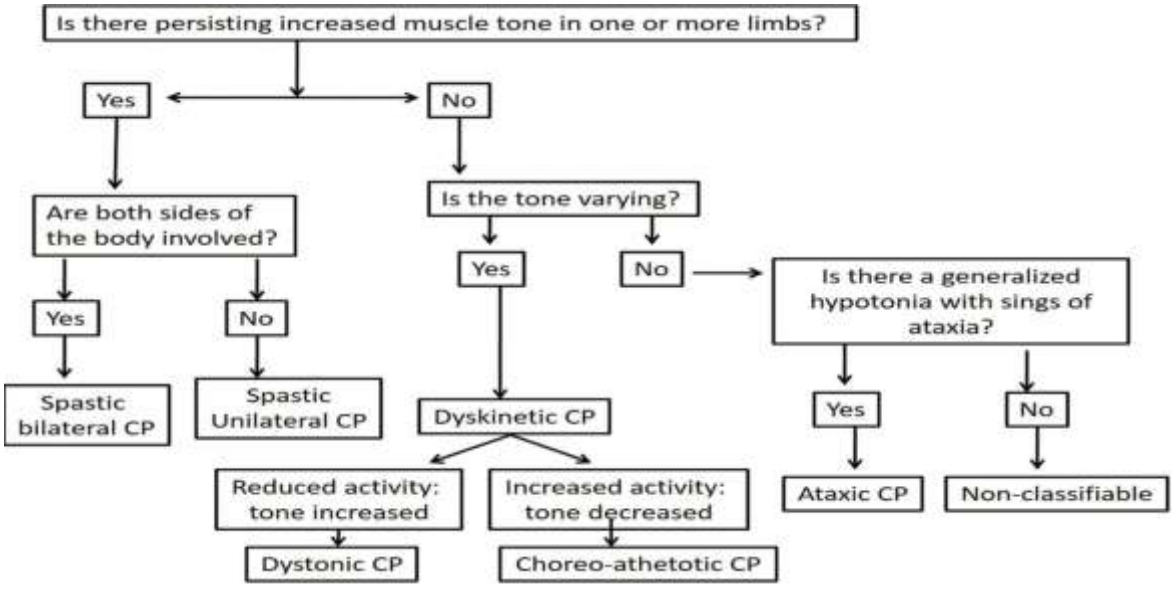
MANAGEMENT OF MOVEMENT DISORDERS IN CP
Medications used for dystonia are:
1. Trihexyphenidyl – Anticholinergic. Starting dose of 0.1–0.2 mg/kg/day, increase once in 3 days to the maximum dose of 1 mg/kg/day (total-max dose (total-max dose kg–30 mg/day and more than 10 kg–60 mg/day[60,61]. can be tried with monitoring adverse effects). The main side effects are dry eyes and mouth, gastrointestinal disturbances, urinary retention, and behavioral disturbances
2. Tetrabenazine – dose 0.5 mg–4 mg/kg/day. In 2 or 3 divided doses, increase once in 3 days. Side effects include drowsiness, parkinsonism, depression, insomnia, nervousness, anxiety, and akathisia
3. Baclofen (in high doses 1 mg/kg /day reduces dystonia)
4. Levodopa (Syndopa) – start at 0.5 mg/kg/day up to 10– 20 mg/kg/day)
5. Benzodiazepines (e.g., diazepam – 0.12–0.8 mg/kg/day and clonazepam – 0.01–005 mg/kg/day)
6. Deep brain stimulation.

REHABILITATION: PHYSIOTHERAPY AND OCCUPATIONAL THERAPY Therapy program
1. Infant-stimulating advanced postural equilibrium and balance reactions to provide head and trunk control
2. Toddler and preschool-stretching the spastic muscles strengthening the weak ones and promoting mobility
3. Adolescent-improving cardiovascular status.

Therapy methods
1. Bobath neurodevelopmental therapy. This is the most commonly used therapy method in CP world-wide. The aims of this therapy are to normalize muscle tone, stimulate normal movements, and inhibit abnormal primitive reflexes. It uses reflex inhibitory positions to decrease tone and promote the development of advanced postural reactions by stimulating key points of control.[61,62]
2. Hand-arm bimanual intensive training (HABIT) for hemiplegic CP where the child is trained to use both hands together through repetitive tasks such as drumming, pushing a rolling pin, and pulling apart construction toys (Legos).
3. Constraint-induced movement therapy (CIMT) involves restraint of the unaffected limb to encourage the use of affected limb during the therapeutic tasks. The restraint may be by the use of casting or physically restraining by holding the normal hand.[63,64]
4. Context-focused therapy involves changing the environment rather than the child's approach. 5. Goal-directed functional training lays emphasis on activities based on goals set by the child using a motor learning approach.

Flow diagram showing Surveillance for Cerebral Palsy in Europe (SCPE) classification of cerebral palsy. Hierarchical classification tree of sub-types (adapted from DMCN2000).

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494



OCCUPATIONAL THERAPY IN CP

As CP can affect children in very different ways, the occupational therapist will start with a full assessment. The focus of the assessment will be as much about understanding the child's abilities as understanding what they are finding difficult and why.[65,66] During the assessment, the occupational therapist will also want to gain an understanding of the child's own goals as well as the goals of their parents, carers, or school. The occupational therapist will provide tailored advice once information obtained during assessment. Below are some examples of how an occupational therapist can assist:

• Improve the child's skills by adapting tasks, teaching, and training or advise on appropriate assistive technology to maximize independence and increase participation[67,68]

• Provides structural building changes and/or equipment in home and schools to facilitate safe access

• Facilitate access to the school curriculum and support school staff in understanding how to best support the child's education[69,70]

• Provides advice on equipment and techniques to maintain postural alignment, to reduce the risk of fixed postural changes such as splinting, supportive seating, and positioning while sleeping.

EXERCISES USED IN OCCUPATIONAL THERAPY

Occupational therapy involves using functional activities to progressively improve functional performance. Occupational therapy exercises focus on the following skill areas:

• Fine motor control – improves hand dexterity by working on hand muscle strength, finger isolations, in-hand manipulations, arching the palm of the hand, thumb opposition, and pincer grasp. Activities include squeezing a clothespin, playing with water squirt toys, and pushing coins into the slot of a piggy bank[71]

• HABIT: Bilateral coordination

• Upper body strength and stability – play focuses on strengthening and stabilizing the trunk (core), shoulder and wrist muscles through exercises such as crawling and lying on the prone position while reading

• Crossing the midline – these activities such as making figure eights with streamers and throwing balls at a target to the right or left of center, teach the child to reach across the middle of their body with their arms and legs to the opposite side [72,73]

• To improve visual motor skills, activities that improve hand-eye coordination such as drawing, stringing beads, catching, and throwing a ball

• For visual perception – activities include alphabet puzzles, playing with different shapes, and matching games

• For self-care, activities such as brushing their teeth, getting dressed, and self-feeding are useful.[74,75]

VARIOUS TECHNIQUES TO REACH THEIR GOALS ARE

• Pediatric CIMT – ask the child to use weaker limb while restraining normal limb

• Sensory integration therapy – here advise activities that stimulate various sensations such as the skin by providing different texture experiences; sand, water, dough, and finger painting.[77]

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

ROLE OF BOTULINUM TOXIN AND ORTHOPEDIC INTERVENTION IN CP[17-19]
Quick orthopedic examination includes
1. Gait and gross motor function classification system (GMFCS) grading
2. Analysis of range of motion and joint contractures of various joints
3. Motor strength assessment
4. Assessment of torsional deformity
5. Upper limb and spine examination.

PATIENT SELECTION FOR BOTULINUM TOXIN
1. Favorable factors
a. Focal goals with specific anticipated functional benefits
b. Increased dynamic muscle stiffness
c. Muscular hypertonia with a functional goal.
2. Negative factors
a. Severe fixed contractures
b. Bony torsion and joint instability
c. Bleeding disorders
d. Too many target muscles – consider other treatment options, or prioritize.

TIMING OF TREATMENT FOR BOTULINUM TOXIN
• For the lower extremity, early treatment is preferable: 1–6 years of age
• For the upper extremity: More than 4 years of age
• Treatment during the dynamic phase of motor development maximizes the chance of permanent modification of the disease
• Early treatment may allow postponement, simplification or even, occasionally, avoidance of surgery
• Later treatment can still be valuable in terms of pain relief, ease of care, and functional goals such as sitting or standing.

RECOMMENDED SAFE DOSE OF BOTULINUM TOXIN
1. Range (U/Kg body wt.): 1–20 U
2. Maximum total dose (U): 400 U 3. Range maximum dose/site (U): 10–50 U.
We did study Koushik et al. [20] there is no difference in outcome with the administration of injection botulinum toxin manual versus ultrasound-guided for lower limb muscle spasticity

PREVENTION
Prevention
PREVENTION OF CP
Primary prevention – preventing the occurrence of CP
1. Health promotion
A. Health education for adolescent girls and improving anemia and nutrition
B. Improvement on the nutritional status of the community
C. Improvement in pre-natal, natal, and post-natal care
D. Optimum health-care facility and infrastructure
E. Awareness regarding developmentally supportive neonatal care. [78,79]
2. Specific protection
A. Rubella immunization for girls
B. Folic acid supplementation during pregnancy
C. Universal iodization of salt
D. Prevention of exposure to teratogenic agents and radiation
E. Pre-natal tests such as triple test and quadruple test
F. Universal immunization for all children
G. Administering anti-D globulin to prevent Rhisoimmunization
H. Intrapartum fetal monitoring to detect fetal distress
I. Improving immunization coverage and preventing accidents.
Secondary prevention Halting and arresting disease progression by early diagnosis and treatment
1. Newborn thyroid screening
2. Neonatal metabolic screening for a treatable inborn error of metabolisms such as galactosemia and phenylketonuria
3. High-risk newborn follow-up clinics for early detection “at risk babies”
4. Cervical encerlage for cervical incompetence to prevent prematurity
5. Antenatal administration of magnesium sulfate to mothers at risk of preterm delivery before 34 weeks of gestation reduces the risk of CP
6. Therapeutic hypothermia for neonates with hypoxicischemic encephalopathy.[80,81,82]
Tertiary prevention
Tertiary prevention is by preventing complications and maximization of functions by disability limitations and rehabilitation.
1. Assistive technology by equipment or ambulatory devices to improve independence, for example, walking frames, wheelchairs, etc.
2. Administration of botulinum toxin and giving antispasticity medicines to reduce spasticity
3. Refractory error correction and vision stimulation and rehabilitation
4. Communication skills may be enhanced by the use of bliss symbols, talking typewriters, electronic speechgenerating devices, hearing aids, etc[81,82].

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

TREATMENT

Treatment of Motor Disorders in CP

Care for a child with CP is a long-term process, aimed at ensuring the child and their family the best possible quality of life. Such a multi-directional approach includes comprehensive rehabilitation, [83,84]specialist medical care as well as psychological and social support.The most important element of CP treatment is multi-faceted improvement. The major role in this improvement is played by systematic and comprehensive motor rehabilitation, individually tailored to the patient. Rehabilitation is based on so-called neuroplasticity, which is the ability of the nervous system to undergo permanent structural and functional changes in reaction to internal and external stimuli; it provides a foundation for learning and memorizing, as well as a basis for adaptation, developmental and compensation changes. It works in the case of both a damaged and undamaged brain,[85,86]which "learns anew" as the result of rehabilitation. The greatest possibilities of modification occur at the earliest stages of development of the central nervous system (CNS). It is at this stage that the brain demonstrates a high degree of plasticity, which favours compensation of various deficiencies. For this reason, rehabilitation of children with CP risk factors should be started as soon as possible. Motor rehabilitation, ie, kinesiotherapy, involves restoring the loss motor patterns or developing new patterns that can compensate for the irretrievably lost functions through enforced motor activity. This is a major method of treating children with CP. An important rule to be followed in rehabilitation is the "developmental rule", which consists in learning subsequent motor skills that naturally appear at various stages of development, in their physiological sequence. There are many specialist neurophysiological methods of rehabilitation applied in CP. The two leading ones are: neurodevelopmental treatment (NDT, Bobath therapy),[87,88,89] and reflex locomotion treatment (Vojta therapy). Physiotherapy, massage, taping and orthopaedic appliances play an ancillary role in rehabilitation. The most frequent symptom in children with CP is spasticity, that is, a state of enhanced muscle tension, which limits the range of passive and active motion in joints and contributes to developing joint contractures. Spasticity has an adverse effect on the further development of motor functions. It hinders rehabilitation, care for patients and their self-care, causing pain, lower self-esteem and worse quality of life as well as contributing to permanent contractures, joint deformities, bedsores, thrombosis and infections.[89,90] Treatment of spasticity involves systematic rehabilitation, if necessary, assisted by pharmacotherapy, physiotherapy or surgical interventions. Selection of a pharmacological treatment method depends on the intensity and location of the disease. In the case of generalized spasticity, the most frequently applied is general treatment. The main drugs used in this kind of treatment include baclofen – an analogue of gamma-aminobutyric acid (GABA), acting on the spinal cord, and benzodiazepine derivatives, such as diazepam, clonazepam or tetrazepam (these act on the central nervous system by releasing endogenic GABA). In the case of focal spasticity, one of the basic therapies is intramuscular administration of botulinum toxin type A (botulin). Botulinum toxin hinders the secretion of acetylcholine in neuromuscular junctions, resulting in a decrease of tension in the group of muscles subjected to treatment. Multi-level administration of botulinum toxin can be effective in the treatment of generalized spasticity.[89,90] The improvement lasts approximately 3–8 months. At that time, systematic motor rehabilitation is necessary so as to make full use of the botulinum toxin effect. By reducing spasticity, botulinum toxin increases the range of passive and active motion, facilitates posture correction, and reduces discomfort and pain related to enhanced muscle tension, which is also felt during rehabilitation. Treatment with botulinum toxin results in a better quality of life for children with CP, both in the case of focal spasticity being confined to single muscle groups, and generalized spasticity[89,90]. Botulinum toxin can also reduce pain after orthopaedic operations in children with spastic types of CP.81–86 In the case of patients for whom the above methods of spasticity treatment have proved ineffective, neurosurgical operations are performed, among others:

- Continuous intrathecal infusion of baclofen through a pump
- selective dorsal rhizotomy: cutting of 50–75% of the dorsal (afferent) nerve fibres on L1-S1 level; this treatment has a permanent and irreversible effect, reducing spasticity solely in the lower limbs
- selective peripheral neurotomy: cutting some of the fibres of the peripheral nerve innervating a particular muscle/group of muscles; it only affects the spasticity of the muscle innervated by the cut nerve fibres.

Additional problems in cerebral palsy, such as gastroesophageal reflux, nutrition disorders, and constipation, require the use of specialist therapy methods, which are frequently surgical treatments.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

Most recently, the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) published guidelines for the evaluation and treatment of gastrointestinal and nutritional complications in children with neurological impairment.90 A huge role is played by the orthopaedic treatment of osteoarticular deformities. The therapeutic process often includes speech therapy for speech impediments and dysphagia. An important role is also played by the treatment of disorders in the cognitive sphere, and psychotherapy for emotional disorders in a sick child and their family.[90,91]

Novak et al,91 in their systematic review study published in 2013, described systematically the best available intervention evidence for children with CP. The authors evaluated 64 different CP interventions reviewed across 131 intervention outcomes.

The following CP interventions were shown to be effective ("green light go interventions"):

1) botulinum toxin, diazepam, selective dorsal rhizotomy for reducing muscle spasticity,
2) casting for improving and maintaining ankle range of motion,
3) hip surveillance for maintaining hip joint integrity,
4) constraint-induced movement therapy, bimanual training, context-focused therapy following botulinum toxin, home programmes for improving motor activity performance and/or self-care,
5) fitness training for improving fitness,
6) bisphosphonates for improving bone density,
7) pressure care for reducing the risk of pressure ulcers,
8) anticonvulsants for managing seizures.

The following therapies were shown to be ineffective for improved motor activities and self-care in children with CP ("red light stop interventions"): craniosacral therapy, hip bracing, hyperbaric oxygen,
neurodevelopmental therapy, sensory integration.

The first choice in this treatment is pharmacotherapy. The effectiveness of pharmacological treatment of epilepsy in the group of children with cerebral palsy is lower than in the group of children with isolated epilepsy.92 Epilepsy in children with CP is frequently drug-resistant. The course of epilepsy and its treatment is largely dependent on the type and severity of CP. Drug resistant epilepsy is more often observed in children with spastic tetraplegia compared to other types of CP. According to the results of some studies, risk factors for drug-resistant epilepsy in children with CP include neonatal convulsions, intense neuropathological changes in cerebrum or mental retardation.

In the case of drug-resistant epilepsy, one should consider non-pharmacological methods of treatment, which include neurosurgical interventions and the ketogenic diet.

Neurosurgical interventions include operations and neuromodulation therapy. Surgeries can be causal or supportive. Causal therapies involve targeted resection of the epileptic focus and are aimed at freeing the patient of seizures.

Supportive treatment is applied in the case of patients with drug-resistant epilepsy who cannot receive a causal therapy. It includes such methods as hemispherectomy, callosotomy, multiple subpial incisions, resection of the frontal part of the temporal lobe, selective resection of the amygdala and hippocampus as well as minimally invasive surgical techniques.

Neuromodulation techniques include vagus nerve stimulation, trigeminal nerve stimulation, deep stimulation of the brain and reflex stimulation. In the case of patients with drug-resistant epilepsy who are not eligible for neurosurgical treatment, an alternative to pharmacological therapy is the ketogenic diet.[83-91] The ketogenic diet is a specialized diet that involves highly restricted intake of carbohydrates and proteins and a high proportion of fat consumption. The precise mechanism of action of the ketogenic diet is not known, although many possible explanations have been proposed. There are many changes that occur in the body and brain as a result of the diet, but it is unclear which of these alterations is responsible for the anticonvulsant effect. It is becoming more apparent that the ketogenic diet likely works through multiple mechanisms that target fundamental biochemical pathways linked to cellular substrates (eg, ion channels) and mediators responsible for neuronal hyperexcitability. There are currently four ketogenic dietary therapies: the classic ketogenic diet, the modified Atkins diet, the mediumchain triglyceride diet and the low glycemic index treatment. Ketogenic diets are established, effective nonpharmacologic treatments for intractable epilepsy. They should be used in children after two anti-epileptic drugs have failed.

II. CONCLUSION

CP is a chronic motor disorder that various efforts failed to prevent its occurrence. In most cases, the cause is unknown and prematurity remains the commonest risk factor. Children with

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

CP suffer from multiple problems and potential disabilities such as mental retardation, epilepsy, feeding difficulties, vision, and hearing impairments. Screening for these conditions should be part of the initial assessment. The child with CP is best cared for with an individualized treatment plan that provides a combination of interventions. This requires the provision of a number of family centered services. Management is not curative; however, if provided optimally it can improve the quality of life of these children and their families. Physicians, in cooperation with the child, family, and members of a multidisciplinary team, can coordinate a complex care system to the maximal benefit of each child

REFERENCES

[1]. Little WJ. The classic: hospital for the cure of deformities: course of lectures on the deformities of the human frame. 1843. Clin Orthop Relat Res. 2012;470(5):1252–1256. doi:10.1007/s11999-012-2302-y

[2]. Mac Keith RC, Mackenzie I, Polani P. The Little Club. Memorandum on terminology and classification of "cerebral palsy". Dev Med Child Neurol. 1959;1:27–35. doi:10.1111/j.1469-8749.1959.tb08073.x

[3]. Bax M. Terminology and classification of cerebral palsy. Dev Med Child Neurol. 1964;6:295–307. doi:10.1111/j.1469-8749.1964.tb10791.x

[4]. Mutch L, Alberman E, Hagberg B, Kodama K, Perat MV. Cerebral palsy epidemiology: where are we now and where are we going? Dev Med Child Neurol. 1992;34(6):547–551. doi:10.1111/j.1469-8749.1992.tb11479.x

[5]. Bax M, Goldstein M, Rosenbaum P, et al. Executive Committee for the Definition of Cerebral Palsy. Proposed definition and classification of cerebral palsy. Dev Med Child Neurol. 2005;47(8):571–576.doi:10.1017/ S001216220500112X

[6]. Rosenbaum P, Paneth N, Leviton A, et al. A report: the definition and classification of cerebral palsy. Dev Med Child Neurol. 2007;109:8–14.

[7]. Cans C, Dolk H, Platt MJ, Colver A, Prasauskiene A, Krageloh-Mann I; SCPE Collaborative group. Recommendations from the SCPE collaborative group for defining and classifying cerebral palsy. Dev Med Child Neurol Supp. 2007;109:35–38. doi:10.1111/j.1469-8749.2007.tb12626.x

[8]. Surveillance of Cerebral Palsy in Europe. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Dev Med Child Neurol. 2000;42:816–824. doi:10.1017/ S0012162200001511

[9]. Leach EL, Shevell M, Bowden K, Stockler-Ipsiroglu S, van Karnebeek CD. Treatable inborn errors of metabolism presenting as cerebral palsy mimics: systematic literature review. Orphanet J Rare Dis. 2014;9:197. doi:10.1186/s13023-014-0197-2

[10]. Zouvelou V, Yubero D, Apostolakopoulou L, et al. The genetic etiology in cerebral palsy mimics: the results from a Greek tertiary care center. Eur J Paediatr Neurol. 2019;23(3):427–437. doi:10.1016/j.ejpn.2019.02.001

[11]. Hakami WS, Hundallah KJ, Tabarki BM. Metabolic and genetic disorders mimicking cerebral palsy. Neurosciences (Riyadh). 2019;24(3):155–163. doi:10.17712/nsj.2019.3

[12]. 12. Pearson TS, Pons R, Ghaoui R, Sue CM. Genetic mimics of cerebral palsy. Mov Disord. 2019;34(5):625–636.doi:10.1002/mds.27655

[13]. Shevell MI, Bodensteiner JB. Cerebral palsy: defining the problem. Semin Pediatr Neurol 2004;

[14]. (1):2-4. 2. King S, Teplicky R, King G, Rosenbaum P. Familycentered service for children with cerebral palsy and the families: a review of the literature. Semin Pediatr Neurol 2004;11(1):78-86. 14. Taft L. Cerebral palsy. Pediatr Rev 1995;16:411- 418. 4. Nelson K, Grether J. Causes of cerebral palsy. Curr Opin Pediatr 1999;11:487-96.

[15]. Bhushan V, Paneth N, Kiely J. Impact of improved survival of very low birth weight infants on recent secular trends in the prevalence of cerebral palsy. Pediatrics 1993;91:1094-1100.

[16]. Pharoah P, Platt MJ, Cooke T. The changing epidemiology of cerebral palsy. Arch Dis Child 1996;75:F169-173.

[17]. Surveillance of Cerebral Palsy in Europe. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Dev Med Child Neurol. 2000;42:816–824. doi:10.1017/

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1882-1901 www.ijprajournal.com ISSN: 2456-4494

S0012162200001511 Dovepress Sadowska et al Neuropsychiatric Disease and Treatment 2020:
[18]. submit your manuscript | www.dovepress.com DovePress 1515 9. Leach EL, Shevell M, Bowden K, Stockler-Ipsiroglu S, van Karnebeek CD. Treatable inborn errors of metabolism presenting as cerebral palsy mimics: systematic literature review. Orphanet J Rare Dis. 2014;9:197. doi:10.1186/s13023-014-0197-2
[19]. Zouvelou V, Yubero D, Apostolakopoulou L, et al. The genetic etiology in cerebral palsy mimics: the results from a Greek tertiary care center. Eur J Paediatr Neurol. 2019;23(3):427–437. doi:10.1016/j.ejpn.2019.02.001
[20]. Hakami WS, Hundallah KJ, Tabarki BM. Metabolic and genetic disorders mimicking cerebral palsy. Neurosciences (Riyadh). 2019;24(3):155–163. doi:10.17712/nsj.2019.3
[21]. Pearson TS, Pons R, Ghaoui R, Sue CM. Genetic mimics of cerebral palsy. Mov Disord. 2019;34(5):625–636. doi:10.1002/mds.27655
[22]. Surveillance of Cerebral Palsy in Europe. Prevalence and characteristics of children with cerebral palsy in Europe. Dev Med Child Neurol. 2002;44:633–640.
[23]. Platt MJ, Cans C, Johnson A, et al. Trends in cerebral palsy among infants of very low birthweight
[24]. Gupta R, Appleton RE. Cerebral palsy: Not always what it seems. Arch Dis Child 2001;85:356-60.
[25]. Carr LJ, Coghill J. Mimics of cerebral palsy. Paediatr Child Health 2016;26:387-94. 9. Vykuntaraju KN. Cerebral Palsy and Early Stimulation. Tamil Nadu: JP Medical Ltd.; 2014. p. 88-9
[26]. Himmelmann K, Horber V, De la Cruz J, et al; SCPE Working Group. MRI classification system (MRICS) for children with cerebral palsy: development, reliability and recommendations. Dev Med Child Neurol. 2017;59(1):57–64. doi:10.1111/ dmcn.13166
[27]. Hoon AH Jr, Stashinko EE, Nagae LM, et al. Sensory and motor deficits in children with cerebral palsy born preterm correlate with diffusion tensor imaging abnormalities in thalamocortical pathways. Dev Med Child Neurol. 2009;51(9):697–704. doi:10.11 11/j.1469-8749.2009.03306.x
[28]. 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. Am J Neuroradiol. 2019;40(1):162–168. doi:10.31 74/ajnr.A5914
[29]. Papadelis C, Ahtam B, Feldman HA, et al. Altered white matter connectivity associated with intergyral brain disorganization in hemiplegic cerebral palsy. Neuroscience. 2019;399:146–160. doi:10.1016/j.neuroscience.2018.12.028
[30]. Nagae LM, Hoon AH Jr, Stashinko E, et al. Diffusion tensor imaging in children with periventricular leukomalacia: variability of injuries to white matter tracts. Am J Neuroradiol. 2007;28 (7):1213–1222. doi:10.3174/ajnr.A0534 35. Trivedi R, Agarwal S, Shah V, et al. Correlation of quantitative sensorimotor tractography with clinical grade of cerebral palsy. Neuroradiology. 2010;52(8):759–765. doi:10.1007/s00234-010-0703-8
[31]. Hoon AH Jr, Lawrie WT Jr, Melhem ER, et al. Diffusion tensor imaging of periventricular leukomalacia shows affected sensory cortex white matter pathways. Neurology. 2002;59(5):752–756. doi:10.1212/wnl.59.5.752 37. Jiang H, Liu H, He H, et al. Specific white matter lesions related to motor dysfunction in spastic cerebral palsy: a meta-analysis of diffusion tensor imaging studies. J Child Neurol. 2020;35(2)::146–-154. doi:10.1177/0883073819879844
[32]. Papadelis C, Butler EE, Rubenstein M, et al. Reorganization of the somatosensory cortex in hemiplegic cerebral palsy associated with impaired sensory tracts. Neuroimage Clin. 2017;17:198–212. doi:10.1016/j.nicl.2017.10.021 39. Papadelis C, Ahtam B, Nazarova M, et al. Cortical somatosensory reorganization in children with spastic cerebral palsy: a multimodal neuroimaging study. Front Hum Neurosci. 2014;8:725. doi:10.
[33]. 89/fnhum.2014.00725 40. Papadelis C, Kaye H, Shore B, Snyder B, Grant PE, Rotenberg A. Maturation of corticospinal tracts in children with hemiplegic cerebral palsy assessed by diffusion tensor imaging and transcranial magnetic stimulation.

Front Hum Neurosci. 2019;13:254. doi:10. 3389/fnhum.2019.00254

[34]. Bosanquet M, Copeland L, Ware R, Boyd R. A systematic review of tests to predict cerebral palsy in young children. Dev Med Child Neurol. 2013;55(5):418–426. doi:10.1111/dmcn.12140

[35]. Granild- Jensen JB, Rackauskaite G, Flachs EM, Uldall P. Predictors for early diagnosis of cerebral palsy from national registry data. Dev Med Child Neurol. 2015;57(10):931–935. doi:10. 1111/dmcn.12760

[36]. Novak I, Morgan C, Adde L, et al. Early, accurate diagnosis and early intervention in cerebral palsy: advances in diagnosis and treatment. JAMA Pediatr. 2017;171(9):897–907. doi:10.5167/uzh149328 44. Smithers-Sheedy H, Badawi N, Blair E, et al. What constitutes cerebral palsy in the twenty-first century? Dev Med Child Neurol. 2014;56:323–328. doi:10.1111/dmcn.12262 45. Kwong KL, Wong SK, Kwan T. Epilepsy in children with cerebral palsy. Pediatr Neurol. 1998;19(1):31–36. doi:10.1016/S0887-8994 (98)00011-3

[37]. Gururaj AK, Sztriha L, Bener A, Dawodu A, Aepen V. Epilepsy in children with cerebral palsy. Seizure. 2003;12(2):110–114. doi:10. 1016/S1059131102002558

[38]. Kułak W, Sobaniec W. Risk factors and prognosis of epilepsy in children with cerebral palsy in north-eastern Poland. Brain Dev. 2003;25(7):499–506. doi:10.1016/S0387-7604(03)00040-8 48. Mert GG, Incecik F, Altunbasak S, et al. Factors affecting epilepsy development and epilepsy prognosis in cerebral palsy. Pediatr Neurol. 2011;45(2):89–94. doi:10.1016/j.pediatrneurol.2011.03.001

[39]. Wallace SJ. Epilepsy in cerebral palsy. Dev Med Child Neurol. 2001;43(10):713–717. doi:10.1111/j.1469-8749.2001.tb00147.x 50. Bruck I, Antoniuk SA, Spessatto A, Schmitt de Bem R, Hausberger R, Pacheco CG. Epilepsy in children with cerebral palsy. Arq Neuropsiquiatr. 2001;59(1):35–39. doi:10.1590/S0004- 282X2001000100008

[40]. Palisano RJ,Cameron D, Resenbaum PL,Walter SD, Rusell D. Stability of the gross motor function classification system. Dev Med Child Neurol. 2006;48(6):424–428. doi:10.1017/S0012162206000934

[41]. Palisano RJ, Rosenbaum PL, Bartlett D, Livingston MH. Content validity of the expanded and revised gross motor function classification system. Dev Med Child Neurol. 2008;50(10):744 750 . doi:10.1111/j.1469-8749.2008.03089.x

[42]. Elvrum AK, Andersen GL, Himmelmann K, et al. Bimanual Fine Motor Function (BFMF) classification in children with cerebral palsy: aspects of construct and content validity. Phys Occup Ther Pediatr. 2016;36(1):1–16. doi:10.3109/01942638.2014.975314

[43]. Ohrvall AM, Krumlinde-Sundhomr L, Eliasson AC. The stability of manual ability classification system over time. Dev Med Child Neurol. 2014;56(2):185–189. doi:10.1111/dmcn.12348

[44]. Himmelmann K, Horber V, De la Cruz J, et al; SCPE Working Group. MRI classification system (MRICS) for children with cerebral palsy: development, reliability and recommendations. Dev Med Child Neurol. 2017;59(1):57–64. doi:10.1111/dmcn.13166

[45]. Hoon AH Jr, Stashinko EE, Nagae LM, et al. Sensory and motor deficits in children with cerebral palsy born preterm correlate with diffusion tensor imaging abnormalities in thalamocortical pathways. Dev Med Child Neurol. 2009;51(9):697–704. doi:10.11 11/j.1469-8749.2009.03306.x

[46]. 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. Am J Neuroradiol. 2019;40(1):162–168. doi:10.31 74/ajnr.A5914

[47]. Papadelis C, Ahtam B, Feldman HA, et al. Altered white matter connectivity associated with intergyral brain disorganization in hemiplegic cerebral palsy. Neuroscience. 2019;399:146–160. doi:10.1016/j.neuroscience.2018.12.028

[48]. Nagae LM, Hoon AH Jr, Stashinko E, et al. Diffusion tensor imaging in children with periventricular leukomalacia: variability of injuries to white matter tracts. Am J Neuroradiol. 2007;28 (7):1213–1222. doi:10.3174/ajnr.A0534

[49]. Trivedi R, Agarwal S, Shah V, et al. Correlation of quantitative sensorimotor

tractography with clinical grade of cerebral palsy. Neuroradiology. 2010;52(8):759–765. doi:10.1007/s00234-010-0703-8

[50]. Hoon AH Jr, Lawrie WT Jr, Melhem ER, et al. Diffusion tensor imaging of periventricular leukomalacia shows affected sensory cortex white matter pathways. Neurology. 2002;59(5):752–756. doi:10.1212/wnl.59.5.752

[51]. Jiang H, Liu H, He H, et al. Specific white matter lesions related to motor dysfunction in spastic cerebral palsy: a meta-analysis of diffusion tensor imaging studies. J Child Neurol. 2020;35(2)::146–-154. doi:10.1177/0883073819879844

[52]. Papadelis C, Butler EE, Rubenstein M, et al. Reorganization of the somatosensory cortex in hemiplegic cerebral palsy associated with impaired sensory tracts. Neuroimage Clin. 2017;17:198–212. doi:10.1016/j.nicl.2017.10.021

[53]. Papadelis C, Ahtam B, Nazarova M, et al. Cortical somatosensory reorganization in children with spastic cerebral palsy: a multimodal neuroimaging study. Front Hum Neurosci. 2014;8:725. doi:10.33 89/fnhum.2014.00725

[54]. Papadelis C, Kaye H, Shore B, Snyder B, Grant PE, Rotenberg A. Maturation of corticospinal tracts in children with hemiplegic cerebral palsy assessed by diffusion tensor imaging and transcranial magnetic stimulation. Front Hum Neurosci. 2019;13:254. doi:10. 3389/fnhum.2019.00254

[55]. Trabacca A, Vespino T, Di Liddo A, Russo L. Multidisciplinary rehabilitation for patients with cerebral palsy: improving long-term care. J Multidiscip Healthc. 2016;9:455–462. doi:10.2147/JMDH. S88782

[56]. Mundkur N. Neuroplasticity in children. Indian J Pediatr. 2005;72 (10):855–857. doi:10.1007/bf02731115

[57]. Reid LB, Rose SE, Boyd RN. Rehabilitation and neuroplasticity in children with unilateral cerebral palsy. Nat Rev Neurol. 2015;11 (7):390–400. doi:10.1038/nrneurol.2015.97

[58]. Sterling C, Taub E, Davis D, et al. Structural neuroplastic change after constraint-induced movement therapy in children with cerebral palsy. Pediatrics. 2013;131:1664–1669. doi:10.1542/peds.2012-2051

[59]. Klimont L. Principles of Bobath neuro-developmental therapy in cerebral palsy. Ortop Traumatol Rehabil. 2001;3(4):527–530.

[60]. Yalcinkaya EY, Caglar NS, Tugcu B, Ronbaklar A. Rehabilitationoutcomes of children with cerebral palsy. J Phys Ther Sci. 2014;26(2):285–289. doi:10.1589/jpts.26.285

[61]. Lee KH, Park JW, Lee HJ, et al. Efficacy of intensive neurodevelopmental treatment for children with developmental delay, with or without cerebral palsy. Ann Rehabil Med. 2017;41(1):90–96. doi:10.5535/arm.2017.41.1.90

[62]. Tekin F, Kavlak E, Cavlak U, Altug F. 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

[63]. Massagli TL. Spasticity and its management in children. Phys Med Rehabil Clin N Am. 1991;2(4):867–889. doi:10.1016/S1047-96 51(18)30686-7

[64]. Pin TW, Elmasry J, Lewis J. Efficacy of botulinum toxin A in children with cerebral palsy in gross motor function classification system levels IV and V: a systematic review. Dev Med Child Neurol. 2013;55 (4):304–313. doi:10.1111/j.1469-8749.2012.04438.x

[65]. Barwood S, Baillieu C, Boyd R, et al. Analgesic effects of botulinum toxin A: a randomized, placebo- controlled clinical trial. Dev Med Child Neurol. 2000;42(2):116–121. doi:10.1111/j.1469-8749.2000.tb00056.x

[66]. Delgado MR, Hirtz D, Aisen M, et al. Report of the quality standards subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Practice parameter: pharmacologic treatment of spasticity in children and adolescents with cerebral palsy (an evidence-based review). Neurology. 2010;74: 336–343. doi:10.1212/WNL.0b013e3181cbcd2f

[67]. Chung CY, Chen CL, Wong AM. Pharmacotherapy of spasticity in children with cerebral palsy. J Formos Med Assoc.

2011;110 (4):215–222. doi:10.1016/S0929-6646(11)60033-8

[68]. Balaban B, Tok F, Tan A, Matthews D. Botulinum toxin a treatment in children with cerebral palsy: its effects on walking and energy expenditure. Am J Phys Med Rehabil. 2012;91(1):53–64. doi:10. 1097/PHM.0b013e31823caae1

[69]. Lowing K, Thews K, Haglund-Akerlind Y, Gutierrez-Farewik EM. Effects of botulinum toxin-A and goal-directed physiotherapy in children with cerebral palsy GMFCS levels I & II. Phys Occup Ther Pediatr. 2017;37(3):268–282. doi:10.3109/01942638.2016.1150384

[70]. Overgard TM, Kjaersgaard-Hansen L, Soe M, Illum NO. Positive experience with intrathecal baclofen treatment in children with severe cerebral palsy. Dan Med J. 2015;62(1):A4999.

[71]. Wang KK, Munger ME, Chen BP-J, Novacheck TF. Selective dorsal rhizotomy in ambulant children with cerebral palsy. J Child Orthop. 2018;12(5):413–427. doi:10.1302/1863-2548.12.180123

[72]. Msaddi AK, Mazroue AR, Shahwan S, et al. Microsurgical selective peripheral neurotomy in the treatment of spasticity in cerebral-palsy children. Stereotact Funct Neurosurg. 1997;69: 251–258. doi:10.1159/000099884

[73]. Romano C, vanWynckel M, Huls J, et al. European society for paediatric gastroenterology, hepatology and nutrition guidelines for the evaluation and treatment of gastrointestinal and nutritional complications in children with neurological impairment. J Pediatr Gastroenterol Nutr. 2017;65:242–264. doi:10.1097/MPG.0000000000001646

[74]. Novak I, McIntyre S, Morgan C, et al. A systematic review of interventions for children with cerebral palsy: state of the evidence. Dev Med Child Neurol. 2013;55(10):885–910. doi:10.1111/dmcn. 12246

[75]. Trivić I, Hojsak I. Evaluation and treatment of malnutrition and associated gastrointestinal complications in children with cerebral palsy. Pediatr Gastroenterol Hepatol Nutr 2019;22:122-31.

[76]. Johnston MV. Clinical disorders of brain plasticity. Brain Dev 2004;26:73-80.

[77]. Jan MM. Cerebral palsy: Comprehensive review and update. Ann Saudi Med 2006;26:123-32.

[78]. Edneuroaiims: E-learningmodules. Cerebral Palsy and Other Neurodevelopmental Disorders. Available from: https://www. pedneuroaiims.chalopadho.com/s/classroo m/1/chapter/7. [Last accessed on 2020 Jan 09].

[79]. Mercuri E, Barnett AL. Neonatal brain MRI and motor outcome at school age in children with neonatal encephalopathy: A review of personal experience. Neural Plast 2003;10:51-7.

[80]. Surender S, Gowda VK, Sanjay KS, Basavaraja GV, Benakappa N, Benakappa A. Caregiver-reported health-related quality of life of children with cerebral palsy and their families and its association with gross motor function: A South Indian study. J Neurosci Rural Pract 2016;7:223-7.

[81]. Mazurkiewicz- Bełdzińska M, Szmuda M, Matheisel A, 83 Wendorff J, Gniadkowska-Nowakowska A. Epilepsy in cerebral palsy. Comprehensive questionnaire research performed in three different provinces in Poland. Neurol Dziec. 2007;16(32):35–38.

[82]. LaRiviere MJ, Gross RE. Stereotactic laser ablation for medically intractable epilepsy: the next generation of minimally invasive epilepsy surgery. Front.Surg. 2016;3:64. doi:10.3389/fsurg.2016. 00064

[83]. Bandt SK, Leuthardt EC. minimally invasive neurosurgery for epilepsy using stereotactic MRI guidance. Neurosurg Clin N Am. 2016;27(1):51–58. doi:10.1016/j.nec.2015.08.005

[84]. Kovac S, Vakharia VN, Scott C, Diehl B. Invasive epilepsy surgery evaluation. Seizure. 2017;44:125–136. doi:10.1016/j.seizure.2016. 10.016

[85]. Camp C, Smithson WH, Bunker M, Burke T, Hughes D. Impact of vagus nerve stimulation on secondary care burden in children and adults with epilepsy: review of routinely collected hospital data inEngland. Epilepsy Behav. 2015;52(Pt A):68–73. doi:10.1016/j.yebeh.2015.08.026

[86]. Qualmann KJ, Spaeth CG, Myers MF, et al. Pediatric epilepsy surgery: the prognostic value of central nervous system

comorbidities in patients and their families. Child Neurol. 2017;32 (5):467–474. doi:10.1177/0883073816685653

[87]. Rho JM. How does the ketogenic diet induce anti-seizure effects?Neurosci Lett. 2017;637:4–10. doi:10.1016/j.neulet.2015.07.034

[88]. Martin K, Jackson CF, Lewy RG, Cooper PN. Ketogenic diet andother dietary treatments for epilepsy. Cochrane Database Syst Rev.2016;2. doi:10.1002/14651858.CD001903.pub3

[89]. Jekovec-Vrhovsek M. Epilepsy in children with cerebral palsy. East J Med. 2012;17:166–170.