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Management of cerebral palsy through the childhood: How does it work in Serbia?

Tretman cerebralne paralize u detinjstvu: Kako funkcioniše u Srbiji?

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Summary Cerebral palsy (CP) is the most common physical disability in childhood, with prevalence in the general population of 1.5 to 3.0 cases per 1000 live birth. The complete causal pathway to CP is unclear in approximately 80% of cases, but risk factors can often be identified from history of conception, pregnancy, birth, or post-neonatal period. CP is not just a physical disability, so comorbidities are commonly present. It is not only the physical development that is at risk, but also the optimal development of children with CP as a whole, including their psychological, social, emotional and cognitive development. CP impacts not only the child, but also the whole family, in a complex, long-term and multi-factorial manner. Historically, the diagnosis has been made between the ages of 12 and 24 months, but now it can be made before 6 months corrected age. Early diagnosis includes neuroimaging, neurological and motor assessments. Early diagnosis is crucial for immediate referral to specific early intervention, which is very important for optimizing infant`s motor and cognitive plasticity, as well as for preventing secondary complications. CP is a life-long condition, and the treatment is long-lasting. Physical therapy takes a central place in managing CP. It focuses on function, movement, and optimal use of the child`s potential.

Key words: cerebral palsy, disability, children, physiotherapy intervention

Sažetak Cerebralna paraliza (CP) je najčešći uzrok fizičke nesposobnosti u detinjstvu. U opštoj populaciji javlja se sa učestalošću od 1.5 do 3.0 na 1000 živorođenih. Tačan uzrok CP nije jasan u oko 80% slučajeva, ali se u većini mogu naći faktori rizika vezani za pre, peri ili postnatalni period. CP nije isključivo fizička nesposobnost, već su često prisutni i drugi poremećaji. Optimalan razvoj deteta (psihološki, socijalni, emocionalni i kognitivni), takođe je u riziku. CP ne pogađa samo dete, već i njegovu porodicu, u svim segmentima života. U bliskoj prošlosti, preciznu dijagnozu CP teško je bilo postaviti u prvoj godini života, ali sada je to moguće i pre 6. meseca (korigovani uzrast). Rana dijagnoza podrazumeva primenu neuroimidžing tehnika, neurološku procenu i procenu motorike. Rano postavljanje dijagnoze važno je za što raniji početak specifične terapijske intervencije koja ima za cilj optimizaciju detetovih motoričkih i kognitivnih potencijala i prevenciju sekundarnih komplikacija. CP je trajno stanje, te je samim tim i tretman dugotrajan. Centralnu ulogu u tretmanu dece sa CP ima fizikalna terapija čiji je osnovni cilj maksimalno poboljšanje pokretljivosti i funkcionalnosti deteta u granicama njegovih mogućnosti.

Ključne reči: cerebralna paraliza, nesposobnost, deca, fizikalna terapija

INTRODUCTION

The term “Cerebral palsy” is an umbrella term used to describe a group of different motor impairments caused by damage to the developing brain. Terminology and definition of cerebral palsy have been the subjects of debate throughout history (1). The term “cerebral palsy” was first used in the medical literature by Sir William Osler in his monograph “The cerebral palsies of children” in 1889. The discussion about terminology continues today, with the proposition of “cerebral palsy spectrum disorder” now suggested as a better and more accurate phrase (2). The current definition of cerebral palsy reads as follows: “Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing activity limitation that is attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, behavior, epilepsy and by secondary musculoskeletal problems” (3). This definition is in alignment with the World Health Organization’s (WHO) International Classification of Functioning, Health and Disability (ICF) framework. It highlights the impact of the condition on a child’s development, function and life trajectory, as opposed to emphasizing solely the brain malfunction or “disease” component of CP.

CP is a life-long condition that impacts not only the child, but also its entire family in a complex manner. There is no specific cure for CP, so the treatment is based on managing the symptoms. Current management of CP includes a combination of physiotherapy, pharmacological therapies

and surgical interventions. This review offers a current opinion on early detection, classification, and treatment of CP; with comparison to procedures available in the three most relevant institutions for CP in Serbia: Institute of Child and Youth Health Care of Vojvodina (ICYHCV), Novi Sad; Special Hospital for Cerebral Palsy and Developmental Neurology (SHCPDN), Belgrade; and Physical Medicine and Rehabilitation Clinic- Pediatric rehabilitation department- Clinical Centre (PMR) Niš.

CP: EPIDEMIOLOGY, AETIOLOGY, EARLY IDENTIFICATION AND DIAGNOSIS

The estimated prevalence of CP in the general population is 1.5 to 3.0 per 1000 live births (4). In low-middle-income countries estimating rates from 2.9 to 4.0 per 1000 live births, while in high-income countries there have been recent reductions in the birth prevalence of CP and current overall prevalence is 1.6 per 1000 live births (5). The higher prevalence rates are reported in children born preterm or at low birth weight (4, 5). Due to the lack of National registry for CP in Serbia, accurate prevalence of CP cannot be specified.

A number of factors may cause damage to the central nervous system at an early stage of its development. Premature birth, especially before 28 week of gestation, is one of the most prominent risk factors for CP and associated neurosensory disabilities. Among children with CP over 40% are born preterm. Events that cause CP can occur prenatally (70-80%), perinatally (10%) or postnatally (10%). Commonly reported risk factors for CP are (6, 7):

a) prenatal factors (maternal and/or fetal), such as TORCH infections (Toxoplasmosis, Other viruses, Rubella, Cytomegalovirus, Herpes simplex virus), genetic and metabolic disorders, prematurity, multiple births, congenital malformations or birth defects, preeclampsia, placenta praevia, intrauterine growth restriction, encephalopathy, neonatal brain injury such as intraventricular haemorrhage (IVH) and periventricular leucomalacia (PVL), strokes;
b) perinatal factors: placental abruption, non-vertex presentation, prolonged labor, birth asphyxia, post-maturity;
c) postnatal factors: respiratory distress syndrome, neonatal sepsis, meningitis, IVH and head trauma before 2 years.

Establishing an early diagnosis of CP is important in order to ensure early intervention, and thus optimize infant motor and cognitive plasticity, minimize secondary complications and enhance parent and caregiver well-being.

However, a diagnosis of CP has traditionally been made from 12 to 24 months, which is after the optimal time frame for applying early specific interventions to improve functional outcomes.

Recent guidelines for the early identification of infants at risk for CP recommends the use of neuroimaging, Prechtl`s General Movements Assessment (GMA) and the Hammersmith Infant Neurological Examination (HINE), for early detection of CP, before 5 months corrected age. Each of these assessments has been tested in high-risk infant populations demonstrating high sensitivity (Sn) and specificity (Sp) for detecting CP as early as three months corrected age (8).

GMA can be applied from birth onward, but its high predictive power with sn-values from 95% to 98% and sp-values from 89% to 96% in cohorts at high risk for CP, primarily lies in the assessment of fidgety GMs (9,10). In Serbia, this method has been in use since 2007 in ICYHCV and PRM, whereas in SHCPDN it has been in use since 2008.

The HINE is a simple and scorable method designed for assessing infants between 2 months and 24 months of age, with sn-values of 90%. It includes 26 items that evaluate different aspects of neurological function, such as cranial nerves, posture, movements, tone, and reflexes. The HINE is easily performed and accessible to all clinicians; it can be completed in 5 to 10 min. A good inter-observer reliability has been reported, even in inexperienced clinicians (11). HINE is not commonly practiced in Serbia, however, traditional neurological examination, which includes assessment of posture, movements, tone, and reflexes, is sufficient and reliable.

Neuroimaging techniques including cranial ultrasound (CUS) and magnetic resonance imaging (MRI) are the main tools in the diagnosis following neonatal brain injury. MRI indicates damage to the motor areas of the brain with sn-values of 86–89%, but there are still some disadvantages to it (e.g., cost, accessibility, and needs for general anesthetic).

CUS remains in common use because of its clinical utility, wide availability and accessibility, and lower costs compared to MRI. With CUS, it is possible to detect common patterns of preterm brain injury, such as IVH and PVL, nevertheless, sometimes subtle lesions cannot be clearly distinguished. Therefore, serial CUS is widely used for screening, in spite of the fact that approximately one third of preterm infants diagnosed with CP may not have lesions identified by CUS. Sn of routinely used CUS is 74%, and sp is 92% (1). MRI provides better anatomical detail and has the sensitivity to detect subtle white matter injury that may not be detected on CUS. In Serbia CUS is routinely and widely used, whereas MRI is available for unclear CUS findings.

HINE, GMA and neuroimaging address different aspects of the condition such as: pathogenesis- mainly targeted by the assessment of neuroimaging findings, impairment- mainly addressed by HINE, and functional limitation as measured by the quality of movements (GMA). Pooled predictive power of these assessments is greater than 97% of accuracy at the age of three month (11).

CP: CLASSIFICATION AND DESCRIPTION

CP is a heterogeneous condition in terms of etiology, motor type, and severity of impairments. Consequently, CP is described using different classifications: motor type, topography, and motor severity (7,11,12):

***Motor Type*:** Motor types of CP include spastic (85%-91%), dyskinetic (4%-7% (which includes dystonia and

choreoathetosis)), ataxic (4%-6%), and hypotonic (2%) which is not classified in all countries. Dyskinesia, ataxia and hypotonia usually affect all limbs, whereas spasticity is classified topographically.

Topography: The spastic motor type is classified as unilateral (hemiplegia (40%–60%)), affecting one side of the body, or bilateral, affecting both sides of the body. Bilateral spastic CP includes: diplegia (10%–36%), with lower limbs more affected than upper limbs; and quadriplegia (24%–31%), with trunk and all four limbs affected.

***Motor severity*:** Prediction of motor severity of CP from the age of two and up is well established using the Gross Motor Function Classification System (GMFCS), which shows a child's level of gross motor function and mobility according to child's age. This scale is based on the assessment of a child's independence when performing basic motor skills, such as walking or moving with the aid. Evaluation of a patient on this scale allows classification into a particular level of performance (levels I, II, III, IV and V). The survey of the SCPE (Surveillance of Cerebral palsy in Europe) showed that about 40% of children with CP have a severe form of CP, which means that their gross motor function is classified in level IV or V, according to GMFCS. The most commonly used system for evaluating and classification of hands' function is MACS (Manual Ability Classification System), a five level system, analogous to GMFCS. Classification of CP children in all the three sites in Serbia is routinely done by GMFCS and MACS.

CP is a permanent, but not unchanging disorder. Progressive musculoskeletal impairments (e.g. contracture and bony torsion, hip displacement, scoliosis) develop throughout childhood and adolescence. The most prevalent symptom in children with CP that adversely affects muscles and joints of the limbs, causing abnormal movements, is spasticity.

Spasticity is a disabling motor disorder and it is especially harmful in growing children. The known adverse effects of spasticity include: inhibition of movement, longitudinal muscle growth, protein synthesis in muscle cells; limited stretching of muscles in daily activities and development of muscle and joint deformities (13).

Management of spasticity aims to improve functional ability and quality of life for children and their caregivers. It involves multidisciplinary intervention which may include: medications (oral, intrathecal), physiotherapy, occupational therapy, orthoses, surgical interventions (orthopedic surgery, neurosurgery), and pharmacological agents such as botulinum toxin. Injections of botulinum toxin A (BTA) are recommended for localized/segmental (focal) spasticity, especially for lower limbs in order to treat dynamic spastic equinus deformity of the foot. The efficacy of BTA in the management of children with CP has been widely reported in the literature (14). BTA treatment has been in common use in Serbia since 2001 (SHCPDN), 2003 (ICYHCV), 2004 (PMR).

Children with CP can demonstrate variety of comorbidities, especially if they have more severe forms of cerebral palsy. Commonly present comorbidities are: chronic pain (27% - 75%) (15) epilepsy (35%), intellectual disability (49%), sleep disorders (23%), behavioral disorders (26%), problems with feeding, swallowing, and bowel motility, poor nutrition and growth, high rates of infection, hearing and visual impairment (16).

MANAGEMENT OF CEREBRAL PALSY

Prevention: Recent reports have demonstrated that treatment with magnesium sulfate of women who are about to deliver at early preterm can prevent cerebral palsy (17). Also, it has been found that therapeutic hypothermia for newborns with hypoxic-ischaemic encephalopathy was followed by reduction in severity of neurological impairments. Many clinical trials are currently in progress with promising signs of efficacy in early-phase, such as administration of melatonin or creatine during the risk pregnancy, thyroid hormone and gene therapy at preterm birth, stem cells at term age, etc. (18).

As specific "cure" for CP is not available, current treatment is based on managing symptoms and associated comorbidities. Treatment includes physiotherapy, combined with pharmacological and surgical interventions. A multidisciplinary approach is recommended. The team usually consists of physiatrist, physiotherapist, occupational therapist, speech and language therapist, psychologist, neurologist, pediatrician, orthopedic surgeon, neurosurgeon, an orthodontist.

***Early intervention* focuses** on the promotion of achieving certain milestones in any affected developmental domain. Motor interventions targeting fine and gross motor skills are often prescribed for infants at risk of, or diagnosed with, CP. Children with CP achieve most of their potential in the first two years, and by the age of 5 they can reach 90% of their gross motor potential (19). First 2 years of life are the critical period for development of corticospinal tract, with great neuroplasticity. Neuroplasticity is the capacity of the brain to recover after injury, and it can occur at all ages, yet, the developing brain has greater capacity for change. Early interventions during this period help neurogenesis and synaptogenesis, protect neurons and promote the secretion of growth factor in the brain. Because of that, the early interventions are vital for optimizing outcomes.

After the initial period of 2 years, individual lifelong rehabilitation is required, with interventions based on the limitation in motor function, activity, participation, musculoskeletal impairments and comorbidities.

***Physiotherapy treatment*:** The overall aim of treatment is to maximize function and minimize incapacity, as well as to adapt the child's environment in a way which ensures their fullest possible participation in society, thereby increasing autonomy and empowerment (20).

There are three main theoretical models that focus on physiotherapy treatment for children with CP:

1. Family-Centered model: Therapeutic interventions for children with CP should be based not only on the perception of the child's disability and the associated consequences, but also on the child's own motivation, the family's expectations, and the support they receive. This approach is known as Family-Centered Service (FCS) and it focuses on patient-centeredness with the

goal of enhancing and optimizing capabilities, ensuring that the family and child have opportunities to participate in clinical decision making.

2. Model based on The International Classification of Functioning, Disability and Health (ICF), a child and youth version (ICF-CY). It focuses on health rather than the consequences of disease or disability. Interventions are designed to target body function/structure deficits, activity limitations and improvement of functional skills, and encouragement of participation in age-appropriate settings.
3. Motor learning and task specific functional activity: These are processes based on child`s ability to learn and should be emphasized in physiotherapy interventions. Children learn cognitive and motor skills by training and through reasoning. Physiotherapy is focused on motor learning and based on movement. The movement patterns and the movement strategies used by a CP child to achieve its goals are its own solutions to the motor problem in interaction with the environment.

The key ingredients for effective treatment constitute a high training intensity combined with meaningful, goal-directed and task-specific training. To be as effective as possible, the physiotherapy intervention should be: timely, intensive, ongoing, and family-centered (21).

There are many treatment approaches for children with cerebral palsy. Some of them are: neurodevelopmental therapy by Bobath, Vojta therapy, conductive education by Peto, strength training, constraint-induced movement therapy. However, there is no evidence that any of these treatments methods is superior to another. Many alternative therapies such as hydrotherapy, hippo-therapy, robotic therapy, may also be incorporated into the rehabilitation treatment (22, 23, 24).

One of the most commonly used treatment approaches for motor disorders and disturbances of posture and movement in children and adults is Bobath approach. This is a "hands-on" approach, which involves three primary treatment techniques: inhibition, facilitation, and specific sensory stimulation. Although this approach is widely used, there is relatively little published research on its efficacy, with controversial results and there is no concrete evidence of significant effects of neurodevelopmental treatment when applied to children with cerebral palsy (25).

Before starting any kind of treatment, it is very important to establish the goals of that treatment. Goals need to be specific, relevant, measurable and clearly defined. Setting these goals should be done by professionals in partnership with the child`s family, taking into account all aspects of both the child's and the parent's activities. Parents need to be well-informed about intervention options, and they need to be listened to, with respect to their goals for their child's development.

When choosing the best treatment option for every child, it is important to focus on what *child can do,* rather than what *child cannot do*. This should be estimated according to child's developmental stage and current functional ability. Therapy must be suited to the needs and abilities of every single individual. Professionals should always have in mind developmental and functional goals, instead of only addressing impairments.

Many of the treatment methods are available in all the three sites in Serbia (shown on table 1.). Treatment is carefully tailored according to child's developmental stage and current functional ability. Real goals of interventions are defined in partnership with parents. Management of CP is conducted by multidisciplinary team, according to ICF framework.

Table 1. Treatment options for children with cerebral palsy in Serbia (in three sites)

Tabela 1. Vrste tretmana za decu sa cerebralnom paralizom u Srbiji (u tri centra)

Treatment options Vrste tretmana	Novi Sad – ICYHCV Novi Sad - IZZIDOV	Belgrade – SHCPDN Beograd - SBCPRN	Nis – PMR Clinic Niš - Klinika za FMR
Spasticity (focal) BTA Fokalni spasticitet BTA	In common use since 2003 Primenjuje se od 2003. god	In common use since 2001 Primenjuje se od 2001. god	In common use since 2004. Primenjuje se od 2004. god
Spasticity- Intrathecal baclofen Spastictet – intratekalna aplikacija baklofena	Not available Nedostupno	Not available Nedostupno	Not available Nedostupno
Spasticity- SDR Spasticitet - SDR	Not available Nedostupno	Not available Nedostupno	Not available Nedostupno
Orthopedic surgery: (muscle/tendon) Ortopedska hirurgija na mišićima i tetivama	Available Dostupno	Available Dostupno	Available Dostupno
Orthoses, braces, walking aids Ortoze i druga pomagala	Available Dostupno	Available Dostupno	Available Dostupno
NDT NRT	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi
Vojta therapy Vojta metoda	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi
CIMT Tretman za ruku i šaku (hemipareza)	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi
Stretching exercises Vežbe istezanja	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi
Parental education Edukacija roditelja	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi
Occupational therapy Okupaciona (radna) terapija	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi
Speech and language therapy Logopedski tretman	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi	Routinely done U rutinskoj upotrebi
Hydrotherapy Hidroterapija	Available Dostupno	Available Dostupno	Available Dostupno

List of abbreviations / Lista skraćenica:

ICYHCV- Institute of Child and Youth Health Care of Vojvodina

IZZDIOV- Institut za zdravstvenu zaštitu dece i omladine Vojvodine

SHCPDN- Special Hospital for Cerebral Palsy and Developmental Neurology

SBCPRN- Specijalna bolnica za cerebralnu paralizu i razvojnu neurologiju

PMR- Physical Medicine and Rehabilitation

FMR- Fizikalna medicina i rehabilitacija

SDR- Selective dorsal rhizotomy / selektivna dorzalna rizotomija

BTA- Botulinum toxin (type A) / botulinski toksin (tip A)

NDT- Neurodevelopmental treatment

NRT- Neurorazvojni tretman

CIMT- Constraint- induced movement therapy

CONCLUSION

Based on comparison of this review's author's personal experience to the data from the relevant literature concerning early detection, diagnosing, classification and treatment for CP, it could be concluded that current management of CP in Serbia is almost up to date. Diagnosis of CP is usually made in the first year, mostly before the 6th month of life. At each of the 3 relevant health institutions dealing with CP in Serbia, there are at least two well-trained and experienced clinicians for GM Assessment. CUS is widely available and routinely done, while MRI is done on demand when CUS is indiscernible. HINE is not a standard procedure, however, traditional neurological examination is sufficient and reliable. Severity of CP is routinely classified according to GMFCS and MACS. All infants at risk have access to early treatment. Rehabilitation of children with CP is conducted in line with ICF by multidisciplinary team. At each of 3 sites there are numerous treatment options.

The main obstacle in management of CP in Serbia is the lack of a National registry for CP. Creating CP registry could be helpful for answering questions about the prevalence and characteristics of CP, monitoring and reporting the changing rates of CP, gaining further understanding about the causes, evaluating preventive strategies, and assisting in planning services for children with CP throughout their lives.

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