REVIEW

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Cerebral Palsy: An Overview

Serebral Palsi: Genel Bakış

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ABSTRACT

Cerebral palsy (CP), the most common cause of disability in childhood, was first described in 1861 by the English orthopedist William Little. CP, which has been expressed in different forms for many years, has been defined in 2006 by an international consensus as "a group of permanent disorders of the development of movement and posture, causing activity limitation that are attributed to non-progressive disturbances that occurred in the developing or fetal brain". CP still remains the most common cause of childhood disability with a prevalence of 1.7-3.1 per 1.000 live births. Today, there are increasing publications stating that risk factors in the aetiology of CP can be traced back to pre-conception period. However, when risk factors considered, prenatal factors appear as the main cause with a weighted rate of 75%. As our knowledge on etiology mounted up, studies on prevention procedures also accelerated. CP is a clinical diagnosis. Therefore, being alert for risk factors is the first and most important step. CP treatment is planned with an integrative approach together with rehabilitation exercises, medical and surgical treatments. The main goal of programs are to enable children to reach their maximum capacity. Despite the technological advances in medical diagnosis and treatment protocols, CP remains to be the most common cause of paediatric disability in childhood. Considering aspects like risk factors, aetiology, prevention measures, diagnosis and management; there are many questions that need answers.

Keywords: Cerebral palsy, diagnosis, management, risk factors, botulinum toxin A, rehabilitation

ÖZ

Çocukluk çağının en sık görülen disabilite nedeni olan serebral palsi (CP) ilk kez 1861 yılında İngiliz ortopedist William Little tarafından tanımlanmıştır. Uzun yıllar boyunca farklı biçimlerde ifade edilerek günümüze ulaşan CP tanısı, 2006 yılında uluslararası bir konsensüs ile "gelişmekte olan fetal veya infant beyin dokusunda sabit hasar sonrası görülen ve aktivite sınırlaması ile sonuçlanan, postür ve hareketin normal gelişiminde duraksamaya yol açan kalıcı bozukluklar grubu" olarak tanımlanmıştır. CP günümüzde her 1,000 canlı doğumda 1,7-3,1 prevalans ile hala en sık görülen çocukluk dönemi disabilite nedeni olmaya devam etmektedir. Bu rakam ülkenin gelişmişlik düzeyi arttıkça düşmektedir. Günümüzde CP etiyolojisinde risk faktörlerinin konsepsiyon öncesine dek uzanabildiğini söyleyen yayınlar artmaktadır. Bununla birlikte; ana neden olarak prenatal faktörler %75 gibi ağırlıklı bir oran ile karşımıza çıkmaktadır. Etiyoloji hakkında bilgilerimiz arttıkça korunma prosedürleri üzerine çalışmalar artmaya başlamıştır. CP klinik bir tanıdır. Bu nedenle risk faktörleri açısından alert olmak ilk ve en önemli adımdır CP tedavisi rehabilitasyon uygulamaları, medikal ve cerrahi tedaviler ile birlikte bütünleyici bir yaklaşımla planlanır. Tedavide temel hedef fonksiyonelliği artırarak çocukları sosyal hayata entegre edebildiğimiz maksimum kapasitelerine ulaşmalarını sağlamaktır. Tıbbi tanı ve tedavilerdeki tüm teknolojik ilerlemeye rağmen CP prevalansı beklenen azalmayı göstermemektedir. Bu nedenle risk faktörleri, etiyoloji, önleyici yaklaşımlar, teşhis ve tedavi gibi unsurları göz önüne alındığında; cevaplanması gereken birçok soru olduğu akılda tutulmalıdır.

Anahtar Kelimeler: Serebral palsi, tanı, tedavi, risk faktörleri, botulinum toksin A, rehabilitasyon

Introduction

Cerebral palsy (CP), is not a defined, separate disease classification, but an umbrella term. The term was first described in 1861 by the English orthopedist William Little. Little has correlated a difficult labour and neonatal hypoxia with limb spasticity and consequential musculoskeletal deformities (1). Although it was first described as a sequela of difficult postpartum hypoxia, we now know that this observation explains a very limited group. CP, which has been expressed in different forms for many years, has been defined in 2006 by an international consensus as "a group

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of permanent disorders of the development of movement and posture, causing activity limitation that are attributed to non-progressive disturbances that occurred in the developing or fetal brain" (2).

Today, CP still remains as the most common cause of childhood disability with a prevalence of 1.7-3.1 per 1.000 live births. The figure decreases as the development level of the country increases (3,4).

Etiology and Risk Factors

For more than 100 years, the main etiology of CP was believed to be prolonged labour. The outcome was tried to be explained by relating it to hypoxia during or after birth. However, despite significant improvements in medical facilities, birth comfort and postpartum care; over the years the incidence of CP did not decrease as expected (5). Due to this fact, researchers keep conducting epidemiological studies worldwide.

Considering risk factors, it should be kept in mind that not every baby with risk factors results in diagnosis of CP. Data certifies that, approximately 55% of children diagnosed with CP before the age of 1 years did not meet the diagnostic criteria at the age of 7 years (6).

Today, there are increasing publications stating that risk factors in the aetiology of CP can be traced back to pre-conception period. Studies indicate that even maternal sociodemographic characteristics and reproductive history are associated with CP (7,8). However, when risk factors considered, prenatal factors appear as the main cause with a weighted rate of 75%. This figure is followed by risk factors of infantile and neonatal periods with 10% and 18%, respectively (5,9).

Studies have shown that the frequency of defects in brain development are correlated with gestational week. Gestational week (<32 weeks) and birth weight (<2.500 g) and incidence of damage are inversely related to each other (10,11,12).

Prevention

As our knowledge on etiology mounted up, studies on prevention procedures also accelerated.

Therapeutic hypothermia: Therapeutic hypothermia applications within 6 hours of birth is aimed to prevent ischemic damage by inhibition of inflammatory cascades and apoptotic cellular processes. It has been estimated that 1 out of 8 new-borns to whom this method is applied is prevented from developing CP symptoms (13,14).

Caffeine: Caffeine is also an agent in trial as a prevention measure. Caffeine for apnea of prematurity trial results indicates caffeine reduces the incidence of CP in very low-birth-weight infants (13,15).

Corticosteroids: When steroid administrations are considered adverse data due to administration time is available. Literature dictates warnings for the use of steroids for the prenatal and postnatal period. While the prenatal betamethasone administration in preterm infants is found to reduce the PVL, early (<8 days) postnatal steroid administration is associated with an increase in CP numbers, despite the pulmonary benefits. In 2010, the American Academy of Paediatrics made recommendations to limit the use of postnatal corticosteroids (13,16,17,18).

Magnesium: Administration of magnesium sulfate during the antenatal period is important for neuroprotection in preterm infants. Magnesium sulfate reduces inflammatory effects through pro-inflammatory cytokine suppression. However, the results are varying for obese mothers. It is wise to state that there is no consensus on the results of the application (13,19).

Clinical Features

CP is a clinical diagnosis. Being alert for risk factors is the first and most important step. Early diagnosis and planning treatment without losing time are of vital importance for these children, to reach the highest physical and cognitive level they can be. The correlation between Paediatricians and Physical Medicine and Rehabilitation (PMR) professionals is one of the most important components of this process. Directing risky babies to PMR specialists as soon as possible will prevent delays in diagnosis and treatment plan (20,21).

The compatibility of motor development with chronological age, persistent primitive reflexes and delay in voluntary motor control are important in terms of diagnosis in infants with prenatal, perinatal and postnatal risk factors. However, considering that spasticity is not fully established before 6 months, athetoid movements are not evident until the age of two, and persistent Babinsky reflexes are not significant, it is difficult to make a definitive diagnosis before the age of two (22,23,24). Therefore, every suspected baby should be included in a rehabilitation program without losing time. MRI and laboratory tests to support the neurological evaluation will accelerate the diagnosis process. As in every other subject, differential diagnosis is also crucial in this aspect. It is possible to reach the final result after excluding progressive neurological diseases, metabolic and genetic disorders. Based on the information above The European Database Group (SCPE) has accepted the optimal age as 5 to confirm the diagnosis (25).

Classification: Clinically, CP can be classified by different methods. According to the extremity involvement, the terms hemiplegia, diplegia, tetraplegia is used; According to the dominant tone disorder, it can be defined as spastic, dyskinetic and ataxic. Balf and Ingram (26), Hagberg et al.

(27) and SCPE (2006) (25) classifications are available as facilitating tools (Table 1). When predominant symptoms are considered, spastic CP is the most common type of CP with a rate of 70-80%. It is presented with increased deep tendon reflexes, pathological Babinsky response and upper motor neuron syndrome symptoms. When ambulant patients are considered scissoring gait and toe walking are common clinical features due to internally rotated and adducted hips and gastrocnemius spasticity. Dyskinetic or athetoid CP (10-20%) which characterized by abnormally slow, writhing movements of the hands, feet, arms or legs that are exacerbated during periods of stress absent during sleep. The rarest type is ataxic CP (5-10%) which impairs balance and coordination. Wide base gait at ambulation and intentional tremors are presented as main characteristics. In the case of mixed symptoms, SCPE suggestions is that the classification should be done on the basis of the predominant symptoms (9,25,28).

Co-morbidities: Different co-morbidities accompanying motor deficits can be seen in children with a diagnosis of CP. Epilepsy (15-90%), mental retardation (40-65%), speech problems (50%), urinary incontinence (30%), malnutrition and growth retardation (27%), and drooling (10%) are the most common symptoms. To achieve desired goals, rehabilitation plans should be done with co-morbidities taken in consideration (6,28,29,30,31,32,33,34,35).

Management

Non-surgical methods: The aim in the rehabilitation of CP is to provide the child with the optimum function that he/she can perform with his/her existing neuromotor capacity and to either reduce existing complications or prevent possible complications. Therefore, each rehabilitation plan is an individually tailored program for each patient.

Rehabilitation is based on term "neuroplasticity". A term that is used to explain the ability of the nervous system to undergo permanent structural and functional changes in reaction to internal and external stimuli. It works in the case of both a damaged and undamaged brain, 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. It is at this stage that the brain demonstrates a high degree of plasticity, which favours the compensation of various deficiencies. Since the neuroplasticity potential is higher in the early stages of life,

Table 1. Classification of CP by Balf and Ingram (26) and SPCE

Ingram's classification	
Type	**Definition**
Diplegia	Spastic paresis occurs especially in lower limbs, 3 or 4 limbs (including quadriparesis syndromes with prevailing lower limb paresis over upper limb paresis).
Hemiplegia	Spastic paresis is unilateral (right or left sided) with predominance of upper or lower limb.
Bilateral hemiplegia (tetraplegia)	Spastic tetraparesis with predominance of upper limb paresis (most severe type of CP in terms of severity of motor disability and co-existing problems).
Ataxia	Muscle tension is reduced, accompanied by hand-eye coordination disorders. Bilateral or with the predominance of one side of the body.
Dyskinesia	Dystonic, athetosic, choreic type of CP, accompanied by trembling or manifesting itself in frequent changes of muscle tone.
Mixed types	The above mentioned types in various combinations.
SCPE classification	
Type	**Definition**
Spastic type	Characterized by enhanced muscle tension, hyperreflexia and pathological reflexes: Split into unilateral spastic and bilateral spastic, without further division into diplegia, tri- or tetraplegia.
Dyskinetic type	Patients perform involuntary, uncontrolled, repetitive, sometimes stereotypical movements; muscle tension, which can be both increased or decreased, and frequently changes over time. The following are identified by SCPE: - Dystonic CP with a predominant faulty posture and enhanced muscle tension (so-called hypertonic-hypokinetic). - Choreoathetotic CP: this type is characterized by quick, uncontrolled, violent, frequently "fragmenting" movements which overlap slow, constantly changing "twisting" movements; tension is usually changeable, predominantly lowered (so-called hypotonic-hyperkinetic).
Ataxic type	Related to motor coordination loss, which results in ataxia, movement smoothness, and trembling; in this type of CP lowered muscle tension is predominant.
CP: Cerebral palsy, SPCE: Surveillence of cerebral palsy in Europe	

it is important to start the treatment of children with CP in the earliest possible period (20,21).

CP management is an integrative approach together with rehabilitation applications, physical therapy modalities, medical and surgical treatments. The main goal in management is to control spasticity, avoid involuntary movements, preserve range of motion, increase function, and enable children to reach their maximum capacity that we can integrate into social life (36).

In rehabilitation programs, neuro-rehabilitative treatment approaches (Bobath, Vojta) form the basis of treatment. Supporting rehabilitation exercises with other modalities such as occupational therapy and speech therapy, and integrating professionals such as psychologists and social workers to the program positively effects the quality and outcome of the treatment. Optimal outcomes require a team approach.

Although it is predicted that intensive treatment programs will lead to more satisfactory results, there is no consensus on the threshold for intensity and duration of rehabilitation programs (37). Analysing rehabilitation programs; it will be noticed that there is no consensus on content, outcomes or long-term gains (38,39,40,41,42,43,44). The reason for the lack of consensus on the results may be attributed to complex clinical feature of the diagnosis and individually tailored nature of the treatment programs. This significant cause result in difficulty in randomization and obtaining the outcomes as numerical data.

Modalities as bracing, kinesiotape, biofeedback and neuromuscular electrical stimulation (NMES) are integral parts of the rehabilitation program.

Bracing: Orthoses prescribed mainly for two different purposes; to prevent deformities and to increase function (45).

Kinesiotape: Kinesiotape was introduced in 1996 by Kenzo Kase to control pain, regulate muscle tone, increase muscle strength, and regulate blood and lymph flow. They are used to increase muscle strength, posture control and spasticity control in the treatment of CP (46).

Biofeedback: Biofeedback application is used to train a single muscle activity in static positions in patients without cooperation deficit. The clinical application of biofeedback to improve a patient's motor control begins by re-educating that muscle by providing visual or audio feedback of electromyogram, positional or force parameters in real time (47,48).

NMES: NMES is an adjuvant treatment for muscle strengthening and spasticity control, which has been shown to improve motor function in CP treatment programs. Similar to rehabilitation programs, there is no consensus on the intensity, duration and contribution of NMES to treatment outcomes (49).

Botulinum toxin: Botulinum toxin type-A (BoNT-A) is a dose-dependent and reversible agent that blocks presynaptic acetylcholine release at the neuromuscular junction. With the increase in clinical experience in recent years, the agent has become the most widely used medical intervention in children with CP. The evidence is that with the appropriate use of BoNT-A in younger children the onset of fixed equinus might be delayed to a small but important degree, permitting later utilization of orthopaedic surgery at optimum age. This means reduction in the serial operations that children used to be exposed between the ages of 2-8 and "birthday syndrome" has become an out of date term. However, the optimism regarding the prevention of contractures generated by the spastic mouse study has never been translated to the clinical practice and almost all of the children still need release surgery. In the case of in non-ambulatory children Botulinum toxin administration is recommended only for pain relief. The agent has the power of increasing the quality of life with the right patient selection. However, there is still no consensus among practitioners on issues such as treatment protocols and application frequency (50,51,52,53,54,55,56,57,58).

Surgical Interventions

Selective dorsal rhizotomy (SDR): SDR is a surgical method that is performed by the incision of the posterior nerve roots. Surgery is applied for spasticity management. The most appropriate age range for CP patients has been determined as 4-6 years. Although undesirable results such as post-operative deep sensory loss, urinary retention, hypotonia and persistent low back pain have been reported, it is an effective surgical method with satisfactory results with the right case selection in lower extremity spasticity (59).

Orthopaedic surgical interventions: Orthopaedic surgical interventions (release surgery, osteotomy, tendon transferring techniques) which are widely performed in the treatment of CP, are applied with the aim of preventing deformities and correcting the existing deformity. For surgical interventions, it would be appropriate to wait until the age of 6 when the child's gait pattern matures. The important aspect to keep in mind is the principle of "performing simultaneous multi-level release surgery in one session". It has been reported that the morbidity of a single session surgical approach is lower compared to multisession surgical approach. When this principle is applied, it has been observed that the results of post-op rehabilitation outcomes are more satisfactory, and the gains

at postural and functional improvements are longer lasting (6,36,60,61).

Conclusion

Despite the technological advances in medical diagnosis and treatment protocols, CP remains to be the most common cause of paediatric disability in childhood. Considering aspects like risk factors, etiology, prevention measures, diagnosis and management; there are many questions that need answers.

Ethics

Peer-review: Externally peer-reviewed.

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