Abstract

Objective: to provide pediatrician with updated information about diagnoses and treatment of cerebral palsy. This articles aims at supplying pediatricians with tools that will help them diagnose and treat cerebral palsy.

Sources: non-systematic review of literature combined with personal experience at the Neurology Unit of Pediatrics Service of Hospital de Clínicas de Porto Alegre - Universidade Federal do Rio Grande do Sul.

Summary of the findings: the cerebral palsy diagnosis and treatment are based on multidisciplinary clinical exam, EEG, CT and MR.

Conclusions: pediatricians are the first physician that see the patient with cerebral palsy. Thus, they should be able to diagnose and treat it.


Introduction

In 1843, Little described chronic encephalopathy in children for the first time. He defined it as a pathology related to different causes and mainly characterized by muscle stiffness. In 1862, the relationship between this condition and abnormal delivery was established. In 1897, Freud suggested the term cerebral palsy (CP), which later had its use strengthened by Phelps, when referring to a group of children that presented quite severe motor dysfunction due to injury of the central nervous system (CNS), similar to or different from the motor dysfunction of Little’s syndrome.1-4

Since the Oxford Symposium, in 1959, the term CP was defined as “sequela of an encephalic aggression, which is mainly characterized by a persistent but not invariable dysfunction of tone, posture and movement. It has its onset early in childhood and it is not only directly caused by this nonprogressive brain injury, but it is also a consequence of the influence of such an injury on neurological maturation”. From that date on, CP was considered as a nonprogressive chronic encephalopathy in children. It constitutes a heterogeneous group, either from the etiologic point of view or regarding the clinic condition, which has the predominant presence of motor symptoms as a common characteristic. Other signs and symptoms can be added to them through different combinations.1,3,4

The epidemiological studies about CP show distinct data.5-7

In 1950, Illingworth considered 600,000 cases in the United States, to which approximately 20,000 are added every year. The incidence in developed countries has varied from 1.5 to 5.9/1,000 live births.1
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There is no specific and official research in Brazil regarding the incidence of people with physical, sensorial or mental impairment. According to Edelmuth, 17,000 new cases of CP occur in Brazil every year.8

The involvement of the CNS in CP cases is due to endogenous and exogenous factors, which are present in all cases in different proportions. Among the endogenous factors, inherited genetic potential, that is, the susceptibility of the brain to presenting an injury should be considered. At the moment of fecundation, the new human being receives a somatic and psychic contingent that corresponds to his/her species, race and ancestors. This is the concept of continuum of injury by Knoblock and Passamanick. Therefore, the individual inherits a specific rhythm of evolution of the nervous system. Together with the potentialities of his/her motor, instinctive-affective and intellectual activity, he/she also inherits the capacity of adaptation, that is, cerebral plasticity, which is the basis for the learning process.3,4

Among these exogenous factors, the type of cerebral involvement depends on the moment at which the agent acts, on its duration and on its intensity. Regarding the moment when the etiological agent affects the developing CNS, there are three different periods: prenatal, perinatal and postnatal.9-11

In a study that analyzed 100 children with CP followed at HCPA from 1979 to 1983, prenatal factors were observed in 35 cases; in ten cases, the most frequent etiologic possibility was the threat of abortion; perinatal factors were reported in 114, asphyxia occurred 38 times; postnatal factors were observed in 10 cases.12

During the prenatal period, the main etiological factors are infections and parasitosis (lues, rubella, toxoplasmosis, cytomegalovirus, HIV); intoxication (drugs, alcohol, tobacco); radiation (diagnostic or therapeutic); injuries (affecting directly the abdomen or fall in a sitting position); maternal factors (chronic diseases, severe anemia, malnutrition, pregnancy at advanced age).

During the perinatal period, it is possible to identify the degree of severe asphyxia through the vital conditions of the newborn (NB), which can be measured by the Apgar score. Severe asphyxia is significant when it is present in successive observations (1', 5', 10', 15', 20'). However, chronic asphyxia that occurs during pregnancy is more important, and it can result in a NB with good vital conditions, but with significant cerebral impairment. Chronic asphyxia is closely connected to placental insufficiency, which causes small or immature fetus.

The association of pre- and perinatal asphyxia is responsible for the greatest contingent of NB’s cerebral involvement. It is the first cause of neonatal neurological morbidity, it leads to CP and it is one of the main causes of death during this period.1,13

The events that cause cerebral involvement are decrease in oxygen supply, due to hypoxemia (decrease in the concentrations of O₂ in the blood), or ischemia (decrease in brain blood perfusion). Ischemia is the most important form of O₂ deprivation. In the neonatal period, hypoxemia and ischemia occur at the same time. Therefore, hypoxic-ischemic encephalopathy is characterized by the association of hypoxemia and ischemia, which, associated with metabolic alterations, especially the ones related to glucose metabolism, lead to biochemical, biophysical and physiological alterations. These alterations are perceived through clinical manifestations that are consequences of the physiological and structural involvement. Probably, cerebral depression is a form of protection in cases of severe hypoxia.1,14,15

Neuropathological alterations of hypoxic-ischemic encephalopathy vary according to age, injury type and form of intervention, resulting in selective neural necrosis, status marmoratus, parasagittal cerebral injury, periventricular leukomalacia or focal and multifocal cerebral ischemic necrosis. Volpe has considered that prenatal hypoxia is responsible for 20% of the cases of hypoxic-ischemic encephalopathy in NBs, perinatal hypoxia is responsible for 35%, and the occurrence of both at the same time is responsible for more than 35% of the cases, with only 10% of the cases for postnatal hypoxia. However, recent animal studies do not show evidence that when hypoxia occurs only during labor, it is able to cause CP, which suggests that the origin of periventricular leukomalacia in hypoxic-ischemic encephalopathy is a pre- and perinatal association of hypoxia. The signs that result from asphyxia during delivery can mean the association of pre- and perinatal hypoxia. It is possible that pre-delivery brain injury causes CP and perinatal hypoxia at the same time. On the other hand, in preterms the postnatal events are more important regarding the pathogenesis of the hypoxic-ischemic encephalopathy than in full-term NBs.1

The prevention of risk factors that predispose to fetal and/or neonatal asphyxia is extremely important for the management and prognosis of cerebral impairment.

The etiological possibilities are shown in Table 1.

In preterm infants, the presence of the germinal matrix in a periventricular position, with its immature vascular network, makes this site prone to asphyxic and hemorrhagic injuries. Arteries of Heubner and lenticulostriate arteries, which nurture this region, are proportionally bigger in the preterm infant than in the full-term NB. Therefore, the former has more intense blood flow in this area, due to the necessity for a greater oxygen supply, which explains why the periventricular region is so sensitive to the oxygen reduction and, consequently, to asphyxia. Thus, there is a close relationship between asphyxia and periventricular and intraventricular hemorrhage in the preterm NB.

Among the postnatal factors, metabolic disorders (hypoglycemia, hypocalcemia, hypomagnesemia);
infections (meningitis due to gram-negative germs, streptococcus and staphylococcus); postinfectious and post-vaccination encephalitis, hyperbilirubinemia (due to mother-fetus blood incompatibility, leading to the condition called kernicterus, with bilirubin impregnation of the basal ganglia); traumatic brain injuries; intoxication (caused by chemicals or drugs); vascular processes (thrombophlebitis, embolizations and hemorrhages); and malnutrition, which interferes in a decisive manner with the development of the child’s brain, should be considered.

Pathological alterations of the anatomy caused by chronic encephalopathy in children are variable because it is a syndrome that can result from several diseases, which occur at several stages of CNS development. Ventricular dilatation with cortical or cortical and subcortical atrophy is the most frequent situation, and it is characterized by a decrease in the number of neurons in a diffuse and localized manner. Porencephaly, which can be unilateral or bilateral, is characterized by the presence of a cavity in the CNS, caused by the absence of nervous tissue. Porencephalic cysts communicate with the ventricular system or with the subarachnoid space, and always occlude an important vessel that produced the infarct, with subsequent tenderness and necrosis of this region. Subdural hematomas, especially those located in the cerebral convexity, evolve in a subacute or chronic manner. A fibrous capsule appears around the subdural hematoma. It is formed by several layers of conjunctive tissue, and it might become totally or partially calcified. Breastfed infant’s birth trauma and traumatic brain injury can be responsible for the occurrence of meningo-cortical adherence, with significant gliosis. Another important aspect is the presence of kernicterus, with golden yellow pigment, which corresponds to the bilirubin impregnation of the basal ganglia. In some cases, the cortex and the cranial nerve nuclei can be impregnated. Bilirubin seems to be toxic for the neuron, causing its destruction.13,16

The basal ganglia can also be affected in cases of status marmoratus and status dysmyelinisatus. In cases of status marmoratus, there is alteration of the brain development regarding the tissues of the brainstem and basal ganglia, and cortical alterations might also occur. The status dysmyelinisatus is characterized by loss of the myelin sheath of the internal capsule, decrease in the number of neurons at the basal ganglia and gliosis. The latter situation is more rare than the former one.13,17

The classification of chronic encephalopathies in children can be done by different methods, taking into consideration the moment of the injury, the site of the injury, the etiology, the symptomatology or the topographic distribution of the injury. We prefer a classification based on anatomical and clinical aspects, since it is more didactic and because it highlights the motor symptom, which is the main element of the clinical condition:

1) spastic or pyramidal;
2) choreoathetoid or extrapyramidal;
3) ataxic;
4) mixed.

Spastic or pyramidal encephalopathy is more frequent. Depending on where it is located and on how extensive it is, its manifestation occurs through monoplegia, hemiplegia, diplegia, triplegia or tetraplegia. The spastic forms present hypertonia of the extensor and abductor muscle of lower limbs, severe hyperreflexia and Babinski’s reflex, and local or generalized strength deficit, depending on how much was affected. The diplegic form, also called Little’s disease, presents very intense spasticity of the lower limbs, which results in the scissors position when the patient tries to stand up, while in the upper limbs the spasticity is slight and, often, it is only detected in situations where there is stress or

**Table 1 - Causes of cerebral palsy**

1 - Prenatal causes
- reduction in partial oxygen pressure
- reduction in hemoglobin concentration
- decreased placental surface area
- altered maternal circulation
- uterine tumors
- umbilical cord knot
- short umbilical cord
- abnormal umbilical cord
- umbilical cord prolapse or clamping

2 - Perinatal causes
**Maternal factors**
- mother’s age
- cephalo-pelvic disproportion
- placental anomalies
- umbilical cord anomalies
- abnormal uterine contractions
- narcosis and anesthesia

**Fetal factors**
- first child
- preterm child
- immature child
- twins
- fetal malformation
- fetal macrosomia

**Delivery factors**
- instrumental delivery
- position anomalies
- duration of labor

3 - Postnatal causes
- anemic anoxia
- anoxia caused by stasis
- anoxemic anoxia
- histotoxic anoxia
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The following aspects are important for the diagnosis of CP:
- history of predominant nonprogressive motor involvement;
- neurological exam able to identify the type of CP;
- EEG in those cases in which there is associated epilepsy;
- CAT and MR to demonstrate cerebral structural alterations.

Treatment

The best treatment for CP is prevention. The great advance in the early identification of the events that lead to brain injury, the appropriate approach to each case, and the possibility of, through the use of neural protective factors, being able to have a positive influence on each case has changed the profile of CP. Today, it depends a lot on taking advantage of the therapeutic windows, which produce better results related to cerebral plasticity. The earlier measures are taken in order to protect or stimulate the CNS, the better will be the response.19

In the past, the care of children with CP was mainly based on personal experience; today, studies with development scales able to quantify responses and reproduce results are being performed.20,21

Patients with CP should be treated by a multidisciplinary team, in which the main therapeutic approach is certainly physical therapy. The different methods used in the field of physical therapy will be employed according to the clinical condition. Among them, the Bobath method is mainly used. It is based on the inhibition of primitive reflexes and pathological patterns of the movements. Phelps method, which is based on the rehabilitation of muscle groups through stages, until motor independence is obtained and complex activities are performed. Kabat method, which is based on the use of proprioceptive stimulation that facilitates motor responses, from reflex responses to voluntary movement. Physical therapy always should take into consideration the stages of normal psychomotor development, and use several kinds of sensitive and sensorial stimulation.1,4,22,23

The occupational therapist and the speech therapist have a very important role since their work is a complement for the physical therapy. The child with CP often needs speech therapy, pedagogical, psychological, ophthalmological and orthopedic care, and certainly, she/he needs important pediatric support.

Osteoporosis typically affects elderly people. However, the importance of the appropriate acquisition of bone mass during childhood and adolescence in order to avoid osteoporosis later in life has been highlighted. Acquisition of inadequate bone mass or loss of bone mass were described in a variety of pediatric diseases, with special attention to CP, mainly in the most severe forms, with intense osteopenia, which may produce fractures, often the first evidence of the problem.

Development of osteoporosis due to long immobility, use of certain medications for long periods, presence of often associated chronic diseases in addition to nutritional deficits, which is quite frequent, significantly increase the risk of fractures in children with CP. In these cases, the use of vitamin D and calcium is essential for bone recovery.15 The diagnosis of osteoporosis is performed through dual-energy x-ray absorptiometry (DEXA).24 Physical therapy
should be directly introduced in this process, mainly in a preventive way, stimulating the improvement of total volumetric bone density, from 11.5%, in children with spastic CP submitted to a program of appropriate therapeutic physical activity.

When epilepsy is associated to CP, the drug treatment is based on the use of anticonvulsants: phenobarbital, phenytoin, carbamazepine, valproate, vigabatrin, lamotrigine or topiramate, with their specific recommendations for each kind of epilepsy, according to recommended doses and intervals. Most cases present good response to monotherapy with phenobarbital in newborns and young breastfed infants; in cases of focal epilepsy, the drugs of choice are phenytoin, carbamazepine or oxcarbazepine; in multifocal forms, valproate is mostly recommended. The most recent drugs, such as lamotrigine, vigabatrin, gabapentin, topiramate and felbamate, are recommended for cases in which refractory epilepsy requires polytherapy. When there is association with West syndrome, the therapy with corticosteroids is recommended. The most frequently used drugs and their doses are displayed in Table 2.

Table 3 shows the drugs used in the treatment of spasticity. Antispasticity medications affect the GABAergic system, the ionic flow, the monoamines, and the glutaminergic drugs. The drugs that affect the GABAergic system are diazepam, baclophen, piracetam and progabide; the ones that affect the ionic flow are dantrolene, lamotrigine and riluzole; the drugs that affect the monoamines are tizanidine, clonidine and beta blockers; and the glutaminergic system is affected by citrate of orphenadrine.25

The association of tizanidine with baclophen presents advantages, without increasing side effects.26 In a meta-analysis with 270 patients in which the effects of tizanidine, baclophen and diazepam were compared, the results showed that those drugs were similar regarding the antispasticity effect, and the muscular strength was better in the group treated with tizanidine.27 Tizanidine used in ICU patients affects spasticity and produces less sedation and better muscular strength.28

Baclophen can be used either through oral or intrathecal administration.29 The intrathecal administration is used in CP with severe spasticity. Its advantages are slowly adjustable doses, higher levels than the oral administration, with fewer side effects. On the other hand, this therapy is not free from complications, nausea, vomiting, sedation, headache, cerebrospinal fluid fistula and catheter migration might occur.30

Samson-Fang, Gooch and Norlin, in 2000, reported the case of a 9-year-old boy, with quadriparetic CP and dystonia, which presented a neuroleptic malignant syndrome, with the use of intrathecal baclophen.31

Gabapentin is highly recommended in cases of spastic CP associated with refractory epilepsy.22,32

Neuromuscular blockades with alcohol, phenol and local anesthetic drugs have been tested for many years. Today, the use of botulinum toxin, in some selected cases, has shown it is useful for the prevention of deformities caused by spasticity, changing the quality of life of children with CP.34-38 The botulinum toxin is a neurotoxin produced by Clostridium, which inhibits the reabsorption of acetylcholine into the synaptic cleft of the neuromuscular junction. The dose is calculated by taking into consideration the child’s weight and the size of the muscle where the drug will be injected. A typical dose for each gastrocnemius muscle, for instance, is four units per kilo of body weight. The efficacy can be observed between 48 and 72 hours, and the effect is kept from two to four months. The treatment interruption depends on the degree of muscular abnormality, patient’s response, and maintenance of the ability obtained.21

The prognosis of the child with CP also depends on the physician’s awareness of the fact that the child is not only one who needs attention. The family also needs medical care. It is necessary to hear and guide the family. The only approach able to provide comprehensive care of CP cases

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose kg/day</th>
<th>Type of seizure</th>
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<tbody>
<tr>
<td>Phenobarbital</td>
<td>2 - 5 mg</td>
<td>Partial and generalized</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>5 - 7 mg</td>
<td>Partial and generalized</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>15 - 20 mg</td>
<td>Partial and generalized</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>30 - 40 mg</td>
<td>Partial and generalized</td>
</tr>
<tr>
<td>Sodium valproate</td>
<td>30 - 80 mg</td>
<td>Generalized</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>2 - 10 mg</td>
<td>Generalized</td>
</tr>
<tr>
<td>Vigabatrin</td>
<td>50 - 100 mg</td>
<td>West syndrome</td>
</tr>
<tr>
<td>Topiramate</td>
<td>2 - 5 mg</td>
<td>Partial</td>
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</tbody>
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<table>
<thead>
<tr>
<th>GABAergic system</th>
<th>Diazepam</th>
<th>Baclophen</th>
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<tbody>
<tr>
<td></td>
<td>Piracetam</td>
<td>Progabide</td>
</tr>
<tr>
<td>Ionic flow</td>
<td>Dantrolene</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td></td>
<td>Riluzole</td>
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<tr>
<td>Monoamines</td>
<td>Tizanidine</td>
<td>Clonidine</td>
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<tr>
<td></td>
<td></td>
<td>Beta blockers</td>
</tr>
<tr>
<td>Glutaminergic system</td>
<td>Orphenadrine citrate</td>
<td></td>
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</table>

Table 3 - Antispasticity medications

<table>
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<tr>
<th>Action on GABAergic system:</th>
<th>Diazepam</th>
<th>Baclophen</th>
<th>Piracetam</th>
<th>Progabide</th>
<th>Lamotrigine</th>
<th>Riluzole</th>
</tr>
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<tbody>
<tr>
<td>Ionic flow:</td>
<td>Dantrolene</td>
<td>Lamotrigine</td>
<td>Riluzole</td>
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is the treatment that focuses on the mother-child, father-mother-child, relative-child, school and community relationships.\(^{39}\)

A couple that plans to have a healthy, intelligent and able child, looks forward to having that child, and creates high expectations regarding this new member of the family, is quite frustrated when the child does not fulfill these expectations, that is, when they realize their child is not what they had idealized. A child with CP causes a deep change in the family habits. In addition, the child often represents a disruptive factor, when the couple’s relationship is not very stable. In these cases, psychological support for the family is very important.

References