The medical management of cerebral palsy

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Abstract

Medical management of cerebral palsy is a complex issue that should be undertaken with the overall aim to improve comfort, function in every day life, self confidence, participation and independence.

Although the main focus is commonly the motor disorder, medical management also encompasses far wider issues including the management of multiple co-morbidities (e.g. epilepsy, visual and hearing impairment, gastro-oesophageal reflux and constipation, learning and behavioural difficulties) which require close multi-disciplinary teamwork.

High muscle tone can be broadly considered as either spasticity, dystonia, or commonly a mixed pattern. Strategies to reduce muscle tone include enteral medication, botulinum neurotoxin, intra-thecal Baclofen, and selective dorsal rhizotomy. However, strength training and reduction of inserted involuntary movements are equally important strategies to improve function.

We also discuss treatable conditions which mimic cerebral palsy, and explore potential future therapies such as stem cells.

Keywords cerebral palsy; dystonia; spasticity

Introduction

Cerebral palsy is a disorder of abnormal tone and posture arising from a non-progressive abnormality of the infant brain. The majority of affected individuals will have increased muscle tone, although in a small minority tone may be normal or reduced. Variants of ataxic and hypotonic cerebral palsy are still recognized, although long term vigilance for progressive neurological disease is particularly important in these cases.

Two main types of hypertonicity are recognized, i.e. spasticity and dystonia, although the two commonly co-exist. Both involve co-contraction of agonist and antagonistic muscle groups, but differ in important ways. Spasticity is defined as a velocity dependent increase in muscle tone, which leads to clinical signs including a spastic "catch", clonus and brisk deep tendon jerk reflexes. Dystonia is more fluctuant, not velocity dependent, and more likely to lead to twisting postures.

The majority of currently available medical therapies are directed at tone reduction, but it is vital to emphasize that hypertonicity is just one aspect of the upper motor neuron syndrome, and that in many children the other associated features of poor motor control or weakness are a greater barrier to function. Great care must be exercised in strategies to reduce muscle tone (particularly in irreversible procedures such as selective dorsal rhizotomy), as some children are reliant on spasticity to functionally compensate for major underlying weakness. In this situation spasticity reduction can lead to an unwelcome reduction in functional performance.

Strategies to improve function, reduce pain, and therefore improve quality of life in young people with cerebral palsy can include:

- Tone reduction to reduce contractures, postural deformity, and discomfort
- Strength training to improve weakness
- Improve co-ordination by better motor control or reduction of involuntary inserted movements

It is vital to emphasize that medical management should always be in the context of input from a multi-disciplinary team. For example, tone reduction without physiotherapy is almost always futile. The above strategies must also be placed within the wider context of management of the associated co-morbidities of cerebral palsy, which commonly include complex multi-organ pathology (see Table 1).

Assessment

Before undertaking any interventions it is essential to perform a detailed baseline physical assessment, including:

- Assessment of tone – the modified Ashworth score is a useful tool to quantify the degree of spasticity in individual muscles. In subjects with predominant dystonia this can be quantified with tools such as the Burke–Fahn–Marsden, Barry–Albright or Dyskinesia Rating Scale. Where spasticity and dystonia appear to co-exist the Hypertonia Assessment Scale can be considered.
- Careful documentation of fixed contractures (sometimes examination under anaesthetic is very helpful)
- Assessment of power (e.g. using the MRC 5 point scale)
- Documentation of functional levels. If time permits the gross motor function measure (GMFM) is a well validated detailed assessment tool able to demonstrate even relatively small changes in function. In a busy clinic the gross motor function classification score (GMFCS) is a quick and useful guide to level of mobility, as is the manual ability classification score (MACS) for upper limb function. Gait analysis where available is very helpful, and should be strongly considered if orthopaedic or neurosurgery is contemplated.

Neurological investigations

Imaging of the brain should be performed in all suspected cases of cerebral palsy. Rarely a space occupying lesion will be discovered that requires urgent neurosurgical assessment (e.g. a brain tumour, or arachnoid cyst obstructing CSF flow causing hydrocephalus). Although as many as 20% of children with cerebral palsy are known to have normal imaging, it should nevertheless raise clinical suspicion of the possibility of an alternative diagnosis, some of which are treatable, including:

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Associated co-morbidities of cerebral palsy

Neurological	Epilepsy, hydrocephalus, visual and hearing impairment
Behavioural and learning	Sleep disturbance, depression, autistic features, learning difficulties, vulnerability
Gastro-intestinal	Difficulty swallowing, gastro-oesophageal reflux, constipation
Bone	Osteoporosis, scoliosis, hip dislocation, pathological fractures
Respiratory	Susceptibility to chest infections and aspiration
Skin	Drooling, pressure sores
Dental	Poor oral hygiene, susceptibility to dental caries

Table 1

- Tethered spinal cord
- Segawa syndrome (also known as dopa responsive dystonia). Although rare this is an important condition not to miss as the motor symptoms are fully reversible with low dose L-dopa.
- GLUT1 deficiency. This is a disorder of brain energy metabolism due to impaired glucose transport into the brain. It can present with seizures, persistent/paroxysmal movement disorders, gait abnormalities and motor developmental delay. Diagnosis can be achieved by either demonstration of a low CSF to plasma glucose concentration (typically less than 0.4, although higher ratios are reported) and mutation analysis of the *SLC2A1* gene. The ketogenic diet can be helpful in both epilepsy and movement disorders due to GLUT1 deficiency.
- Metabolic disease including glutaric aciduria type 1, biotinidase deficiency, mitochondrial disease
- Single gene disorders such as hereditary spastic paraparesis (although onset is only rarely in infancy)

Conventional medical therapies to reduce hypertonicity

Conventional medical therapies to reduce spasticity and/or dystonia can be targeted in four main ways:

1. Direct muscle relaxants
2. Denervation or neuromuscular blockade
3. Central inhibition
4. Reduction of afferent input from the hypersensitive stretch reflex by selective dorsal rhizotomy

Alternatively they can be considered via their route of administration e.g. enteral medications (see Table 2), localized injections (e.g. botulinum neurotoxin), or more general measures (e.g. intra-thecal baclofen or selective dorsal rhizotomy).

Direct muscle relaxants

Dantrolene inhibits calcium release from the sarcoplasmic reticulum of muscle cells. Although generally safe, there are reports of dantrolene associated hepatitis in adults, and therefore it is recommended that liver function tests are monitored prior to and at intervals after starting therapy.

Denervation or neuromuscular blockade

Chemical denervation can be achieved using either botulinum neurotoxin (BoNT) or phenol. BoNT has been in widespread use for over 20 years. In addition to tone reduction, it is also used in cerebral palsy to reduce drooling and correction of strabismus.

The majority of medical use is type A toxin (BoNT-A), which is composed of a heavy and light chain. The light chain interferes with the binding and release of acetylcholine across the muscle junction, thereby resulting in weakness due to chemical denervation. The effect usually lasts 3–4 months, until reinnervation occurs due to progressive nerve sprouting.

The two major drawbacks to BoNT-A are the short term duration of effect, and the need for it to be administered by injection, usually into multiple muscle groups. The majority of injections for children in the UK are performed under sedation (e.g. Midazolam), or with inhaled nitrous oxide. General anaesthesia still has a role, and has the additional advantage of allowing a detailed assessment of fixed contractures. Most experts agree on the need for accurate localization of the muscle. Large muscles (e.g. gatrocnemius) can usually be safely identified on anatomical grounds, but injection of small or deep seated muscles is aided by nerve stimulator or ultrasound guidance. Some experts also stress the need to inject as near to the motor end plate as possible, although others argue that the inevitable diffusion throughout the injected (and adjacent) muscles renders this non-essential.

There are several different commercially available preparations of BoNT-A available in the UK. Differences are claimed by the manufacturers in relation to the degree of protein binding (which may affect the extent of diffusion to adjacent or more widespread muscle groups), but the main thing to highlight to the novice is that the dosage in units per kg varies between the two most widely used products (Botox® and Dysport®). A precise comparison is not published, but as a general guide most clinicians consider a ratio of between 2 and 3 units of Dysport® to 1 unit of Botox®.

Theoretical concerns about BoNT-A include the long term effect on muscle architecture, and there is some data derived

Personal practice of authors for oral medications to treat abnormal tone, posture and inserted movements in children with cerebral palsy

	Spasticity	Dystonia	Dyskinetic movements
First line	Baclofen	Trihexiphenidyl Gabapentin Clonidine L-dopa (first line if considering Segawa syndrome)	Levetiracetam
Second line	Gabapentin Diazepam	Baclofen Diazepam	Tetrabenazine Sodium Valproate Carbamazepine
Third line	Dantrolene Tizanidine	Carbamazepine (particularly helpful in PKD) Dantrolene	Gabapentin Clonidine Diazepam

PKD: paroxysmal kinesogenic dystonia.

Table 2