OUTCOMES IN REHABILITATION FOLLOWING PATIENT SELECTION FOR THE MANAGEMENT OF DISABLING SPASTICITY WITH INTRATHECAL BACLOFEN AND/OR BOTULINUM TOXIN TYPE A

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Involuntary muscle overactivity or spasticity is an increase in muscle tone caused by a neurological insult that creates an upper motor neurone lesion from either a cerebral (e.g. cerebral palsy, acute brain injury, stroke) or spinal cord (e.g. spinal cord injury, multiple sclerosis) aetiology.

Development of spasticity is a complex process, occurring over time, caused by changes in afferent central and peripheral input to the spinal motor neurones, changes in tonic and phasic stretch reflexes that affect spinal excitability, and changes in the intrinsic properties of motor neurones. Depending on the location of the lesion, the muscle overactivity can be focal, multifocal, segmental, multi-segmental or generalized and can become disabling spasticity. The correct treatment, or combination of treatments, is essential to reduce or eliminate the problems and disability caused by the involuntary muscle overactivity, to optimize function, and to prevent secondary complications, such as muscle and soft-tissue shortening (contractures) or skin breakdown.

Many parameters can influence the clinician's choice of treatment for disabling spasticity; whilst physiotherapy and an effective physical management programme remain pivotal to effective management, pharmacological agents are often required and oral medication is frequently utilized first-line; however, side-effects or poor efficacy are commonly reported.

Other treatment options may then be considered, including intrathecal baclofen (ITB) or botulinum toxin type A (BoNT A). ITB is administered by a programmable, subcutaneously implanted drug delivery system with a reservoir and catheter, delivering low doses of baclofen (<1% of the oral dose) directly to the spinal cord, where Gamma-aminobutyric acid (GABA) receptors are expressed at high density. In long-term follow-up studies, ITB has proven to be safe and its effect sustainable over time, with many

individuals demonstrating high levels of satisfaction and continuing to benefit for many years. However, despite the increasing body of evidence documenting the usefulness of ITB in managing spasticity, there is a lack of patient selection tools to aid the clinician in deciding which patients are most likely to benefit from ITB. On the basis of current evidence, the best-established treatment effect of ITB is in reducing spasticity in the lower limbs of patients with spasticity of cerebral or spinal origin who have failed to respond to maximum tolerated or recommended doses of oral antispasmodics. Botulinum toxin (BoNT) is an extremely powerful naturally occurring neurotoxin produced by Clostridium botulinum, a Gram-negative anaerobic bacterium. BoNT type A products are licensed for the treatment of upper and lower limb spasticity in adults and children. BoNT A is injected directly into muscles and causes inhibition of release of acetylcholine at the neuromuscular junction, the clinical effects of which last some months before functional recovery of the injected muscle. Current treatment guidelines for BoNT A recommend that injections should be offered for focal spasticity of the upper and lower limbs. Such recommendations are based largely on extensive safety and efficacy data from well-designed clinical trials in adults with upper-limb spasticity, while there are fewer data reporting the efficacy of BoNT A in clinical trials in adults and children with lower-limb spasticity. Furthermore, treating multi-focal or multi-segmental upper- or lower-limb spasticity may require higher total doses per session than those currently approved for products available in Europe, in order to meet individual clinical needs and goals of rehabilitation therapy. The safety of BoNT A treatment is well-established in both adults and children, across a variety of indications and also at higher dosages for one BoNT A product (incobotulinumtoxinA, Xeomin, Merz Pharmaceuticals, Germany). However, there are some concerns that the administration of higher doses of BoNT A can increase the risk of systemic diffusion, with the development of clinically evident adverse effects and neutralizing antibodies. When faced with a patient with disabling spasticity, however, there remains uncertainty in how to select the most appropriate treatment.

Keywords: rehabilitation, spasticity, botulinum toxin, intrathecal baclofen

Reference

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