7. Dose-Response Relationships in Patients Treated with Botulinum Toxin for More Than Three Years

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Since the introduction of botulinum toxin to clinical medicine in 1978 by Scott, a large number of patients with essential blepharospasm, Meige’s syndrome, and hemifacial spasm have been treated with botulinum toxin. During the first injections, botulinum toxin has proven effective in relieving involuntary facial movements and involuntary blepharospasm. Because immunologic resistance has been reported when larger doses have been used to treat neck dystonias, the sustained effectiveness of botulinum toxin over an extended period needs to be determined. Furthermore, histologic alterations in nerve and striated muscle anatomy and physiology may influence the response to repeated injections of botulinum (as the result of muscle atrophy, fibrosis, axonal collateral sprouting, or myoneural junction alterations).

Our patient population was studied over four years. Dose requirements and duration of action were determined on a clinical basis; if an injection failed to produce at least a 50% improvement in symptoms and no adverse side effects of the toxin were present, a booster injection would be given within two weeks, increasing the dose by 50%.

The dose required to produce the initial clinical effect appeared to increase until the fourth generation of injections and then leveled off. The duration of effect appeared stable and constant through eight generations of injections. The dose requirement for hemifacial spasm was significantly less than that for blepharospasm/Meige’s syndrome (P < .05) and duration of action was significantly longer for hemifacial spasm than for blepharospasm/Meige’s syndrome (P < .05).

8. Method of Administration of Botulinum Toxin Currently Used and Complications

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The methods of administration of botulinum toxin for the various facial spastic diseases are similar. The freeze-dried toxin is available from the Smith Kettlewell Eye Research Institute in San Francisco. The toxin is reconstituted in normal saline, and small nanogram doses are then drawn up into tuberculin syringes for therapeutic use. Normally, toxins are given in four to six sites in approximately spaced subcutaneous tissue in the upper and lower eyelids, and also in some cases in the eyebrows. The toxin is usually placed on top of or into the orbicularis muscle.

Fortunately, virtually no systemic side effects associated with the use of botulinum toxin have been reported so far. However, several local side effects can certainly occur. The most common side effects appear to be related to placement of the injection itself. Ptsosis is the most common side effect noted in the study by Townsend and Borodic, in which almost 10% of patients over a period of time may develop some degree of ptosis, usually lasting anywhere from one to three weeks and then resolving. Other side effects that have been found include diplopia in less than 5%, especially with larger doses, along with ectropion, tearing, dry eye, exposure keratitis, and other less common local effects. Ways to decrease the incidence of side effects are discussed.

9. Side Effects of Botulinum Injection for Lid Spasms—Five Years Experience

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From April 1983 to April 1988, 381 botulinum injections for lid spasms were performed in 106 patients. Sixty-nine patients had bilateral blepharospasm and 37 had hemifacial spasm. Of the 381 injections, 308 were analyzed for complications and side effects during a follow-up visit. There were no systemic effects. All side effects were temporary, and there were no serious complications. Ptsosis was the most frequently encountered problem, occurring after 26 injections (6.8%). Other complications included corneal exposure (8 injections, 2.59%), facial droop (11 injections, 3.57%), diplopia (5 injections, 1.62%), and subtle visual blurring (8 injections, 2.59%). The following were noted once only by history: jaw tension, tearing, brow droop, and crossed eyes. Only 10 injections had minimal therapeutic effect, although a repeat injection was effective in most of these cases. Only 4 patients chose surgical treatment (selective facial nerve divisions) after beginning the injections. We conclude that the local side effects of botulinum injections for lid spasms are mild and always temporary so that the medicine provides very safe relief from lid spasms.

10. Motor Point Determination

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Electrical stimulation of striated muscle by means of a brief pulse of current occurs because the stimulus depolarizes alpha motor axons; muscle fibers are not stimulated directly by the pulses routinely used, all of which are a millisecond or less in duration. Where the impulses arise along the distal course of motor nerve fibers is determined by the position of the cathode and anode (i.e., the path of current flow) and by the anatomy of the distal nerve within the muscle. These arrangements are more complicated when muscles are stimulated noninvasively by electrodes on the skin rather than by indwelling perineural or intramuscular electrodes. A motor point is defined as a small area on the skin over a particular muscle at which the threshold for electrical excitability of that muscle is minimal. With percutaneous electrical stimuli, the muscle is most excitable at its motor point because it is there that current can most easily reach the nerve fibers supplying it. In some muscles, the motor point overlies the entrance of the nerve into the muscle; in others, it is where a motor nerve or its terminal branches happen to be closest to the skin.

Neuromuscular junctions, as recognized by staining motor end plates, are usually situated near the center or equatorial region of each muscle fiber. In any given muscle fascicle, they are restricted to a narrow region termed the innervation zone. Because botulinum toxin blocks neuromuscular transmission by interfering with acetylcholine release from presynaptic vesicles (in motor axon terminals), it is most effective when injected at or very close to the innervation zone. Whereas the innervation zone of certain muscles lies immediately beneath the motor point, that is not the case for all muscles. In the flexor carpi radialis and palmaris longus muscles, fasciculi run parallel to the overlying fascia, and the motor nerve enters perpendicular to the muscle at a point near the center of the deep surface of the muscle, so that the motor point and innervation zones are anterior and posterior to the muscle, respectively. In some muscles, the motor nerve may even be entirely subjacent to the muscle. In summary, the ideal motor point of a muscle is that area of the muscle where the motor nerve enters the muscle and where the motor point appears to differ from the site at which the innervation zone lies. In this respect, the innervation zone appears to differ from the motor point.