Botulinum toxin as a treatment for drooling of saliva

Drooling of saliva, as a consequence of difficulty with swallowing either because of pharyngeal muscle weakness, reduced spontaneous swallowing or incorrdination, is a common and disabling condition which contributes to a poor quality of life and to carer burden. It can be seen in association with a wide number of neurological disorders (Table 1). The parotid, sub-mandibular and sublingual salivary glands account for about 90% of daily salivary production while the lingual and other minor salivary glands secrete about 10%. Normal daily salivary production is 1 to 1.5 litres. The salivary glands are controlled by the autonomic nervous system, mediated by adrenergic and cholinergic nerve endings, and are primarily under parasympathetic control.

In 1822, Justinus Kerner, a German poet and physician, noting the severe dryness of mouth in patients with botulism first suggested that the toxic substance causing botulism might be useful in treating hypersalivation. But it has only been in the last few years that Botulinum toxin Type A (BTXA) has been used for this purpose. BTXA binds selectively to cholinergic nerve terminals and rapidly attaches to acceptor molecules at the pre-synaptic nerve surface. Internalised BTX inhibits the release of acetylcholine from the synaptic vesicles into the synaptic cleft resulting in reduced function of parasympathetic controlled exocrine glands (or reduced muscle contraction in the case of neuromuscular junction). The blockade though irreversible is temporary as new nerve terminals sprout to create new neural connections.

BTXA as a form of treatment for salivary drooling has proved attractive especially as, on the whole, other treatments for drooling have proved attractive especially as, on the whole, other treatments have overall been reported as being reasonably good. However the variables and episodic nature of the problem coupled with fluctuations based on impaired alertness and cognitive dysfunction, reduced physical activity and posture makes accurate assessments difficult. In the relatively few reports that appear in the literature, the injections of BTXA have been made percutaneously into the parotid and in some cases both the parotid and submandibular glands. In almost all reports in the literature the injections have been made blind but in one report the injections were made under ultrasound control to avoid vascular structures and the branches of the facial nerve.

The reported doses of BTXA used vary between 5-40 mu of Botox (Allergan) for each parotid gland and 2.5-15mu of Botox (Allergan) for each submandibular gland. If Dysport (Ipsen) is used the equivalent doses will need to be used. There is an unresolved debate as to the appropriate equivalent dosage between the two products. It has been reported to vary between 1:3 and 1:6, the wide differences are probably because of methodological reasons. The three larger randomised controlled studies that have tried to answer the question have reported bioequivalence ratios of Botox to Dysport of 1:4, 1:3 or below. Trials in patients with cervical dystonia treated with botulinum toxin type B (BTXB) have reported an increased incidence of dryness of the mouth, this may suggest that a smaller dose of BTXB could cause the same effects with reduction in the potential for dysphagia. Trials using BTXB are planned.

The main side effect of this form of treatment is dysphagia.

Table 1: Common neurological disorders associated with drooling of saliva
- Parkinson’s disease and other akinetic rigid syndromes
- Motor neurone disease with involvement of bulbar muscles
- Cerebral palsy
- Post stroke
- Post-traumatic encephalopathy

Table 2: Methods of assessing salivary production and drooling:
- 1-10 visual analogue scale (where 1 is best possible improvement and 10 is the worst possible situation) based on the patient/carer observations
- Counting the number of standard sized paper handkerchiefs used in the course of the day
- Inserting gauze rolls of known weight into the mouth for a short period of time and calculating the difference between the wet and dry weight of the gauze rolls
- Salivary gland scintigraphy

Table 3: Potential side effects of BTX treatment for salivary drooling:
- Dysphagia
- Weak mastication
- Damage to the facial nerve/artery
- Dental caries
- Parotid gland infection

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due to diffusion into nearby bulbar muscles. Mastication can also be weakened due to unwanted weakness of the masseter muscles. These effects would appear to be related to injection placements and dose. EMG guided injection can prevent inadvertent injection into the masseter muscle and improved delivery of BTXA by injecting retrogradely through Stenson’s duct is being investigated and may prove to be a useful procedure. Other potential side effects are listed in Table 3.

In order to prevent the potentially serious side effect of dysphagia it is prudent to initially begin treatment with only between 6 to 14 mu of Botox (Allergan) to each parotid gland (divided into 2 sites) depending on the amount of drooling (Figure 1).

If with this dose the clinical response is felt to be insufficient the procedure may be repeated after 2 weeks. If still ineffective the submandibular glands may then be injected with 5mu of Botox to each gland. The effect of the BTXA is temporary and lasts for between 3-6 months and hence repeat injections are necessary.

References:

INVOS Cerebral Oximeters
State-of-the-Art Neuro Protection

The INVOS Cerebral Oximeter is the first patient monitoring system to noninvasively and continuously monitor changes in the regional oxygen saturation of the blood in the cerebral cortex of the brain.

Use of the system allows medical professionals to monitor changes in cerebral oxygen saturation and take corrective action.

Research indicates that this can prevent or reduce neurological injuries associated with surgery and other critical care situations and, therefore, reduce the cost of care.