Is injection of botulinum toxin type A effective in the treatment of drooling in children with cerebral palsy?

Report by

L Vaile, F Finlay, Community Child Health, NHS House, Newbridge Hill, Bath BA1 3QE, UK; louise.vaile@banes-pct.nhs.uk
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You see a 12 year old boy with cerebral palsy (CP) in outpatients. His mother is concerned about his drooling. He has tried hyoscine patches with little effect. His mother has heard a radio programme about botulinum toxin (BTX-A) injections and asks you whether it would be beneficial.

Structured clinical question

In children with cerebral palsy [patient] is botulinum toxin A [intervention] effective in the treatment of drooling [outcome]?

Search strategy and outcome

Secondary sources: Cochrane Database: 0.

Primary Sources: Medline 1966 to present: botulinum AND drooling AND cerebral palsy; botulinum AND sialorrhoea AND cerebral palsy. Limit = English language. Ten articles; six relevant (two papers by Jongerius *et al*^{2,3} were published in different journals but relate to the same study group of children). See table 3.

Commentary

Drooling is a significant problem in many children with cerebral palsy. In addition to the physical effects, drooling causes psychosocial morbidity by detracting from physical appearance and inhibiting others initiating close contact. The management of drooling may be problematic as anticholinergic drugs cause significant side effects, surgical treatments have associated complications, and behavioural modification techniques have limited use in children with moderate or severe cognitive problems.

Recently botulinum toxin A has emerged as a potential treatment for the management of drooling. Botulinum toxin A blocks the neuromuscular junction by inhibiting the release of presynaptic acetylcholine and this prevents the secretion of saliva. The first trial results, published in 2000,⁷ in adults with Parkinson's disease showed botulinum toxin to be an effective treatment for drooling; subsequently trials have looked at its use in the management of children with cerebral palsy.

Studies involved injection into the submandibular glands, the parotid glands, or both. The submandibular glands produce 60–70% of secreted saliva when not eating or drinking. Outcome measures in the studies were either a reduction in saliva secretion or an improvement in quality of life for the child as a consequence of reduced drooling. In the study by Jongerius *et al*,² injection into the submandibular glands resulted in 64% of children showing a response at 2 weeks, decreasing to 49% at week 24. The parotid glands are more superficial and therefore easier to inject under local anaesthetic; and Savarese *et al*⁶ found that 53% patients showed a marked response to injection. Suskind and Tilton⁵

found that treatment was most effective (80%) when both the submandibular and parotid glands were injected.

Studies used different doses of botulinum toxin A with differing response rates. Bothwell *et al*⁴ used the lowest dose (10 units divided between parotid glands); 3 of 9 children were described as "good responders". Savarese *et al* injected 15 units into each parotid gland; 53% of children showed a "marked improvement in drooling". Higher doses were used in the studies by Jongerius *et al*; a 51–63% reduction in maximal salivary flow rate was achieved in the 2001 study, although the paper does not state whether this reduction in flow rate led to clinical benefit. The studies therefore suggest that the effect of botulinum toxin A may be dose related, with 50 units being the maximum dose used in the study patients.

The duration of effect of botulinum toxin A was variable between individuals and between studies and varied according to the outcome measurement.

Savarese *et al* showed a sustained significant reduction in severity, frequency of drooling, and number of bibs used for 2 months but no significant difference by 3 months. Jongerius *et al*² found that 48% of patients continued to have a clinical response to botulinum toxin A, using the drooling quotient, at 24 weeks, which was the duration of the study. The length of follow up in these studies may have been too short to determine the true duration of effect of treatment in some patients.

Jongerius *et al*² found that 40% patients experienced severe side effects with scopolamine. No significant side effects were reported following administration of botulinum toxin A in this or other studies, although minor effects such as local swelling, chewing difficulties, dry mouth, and transient weakness of mouth closure have previously been reported.

Injection of botulinum toxin A is an invasive procedure and may require a general anaesthetic or sedation in children, depending on their anticipated ability to tolerate the procedure. It is generally performed by oral surgeons who may locate the glands by palpation, but other trained professionals may administer the injections under ultrasound localisation.

CLINICAL BOTTOM LINE

- Intracervical gland injection of botulinum toxin A shows benefit beyond scopolamine patches in many children with cerebral palsy and drooling in non-randomised studies. (Grade C)
- General anaesthesia may be required to administer botulinum toxin A; its effects are time limited. (Grade C)

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Table 3 Effect of botulinum toxin on drooling in children with cerebral palsy

Citation	Study group	Study type	Outcome	Results	Comments	Level of evidence
Jongerius <i>et al</i> (2001) ¹	3 children (11–13 years) CP and severe drooling	Case series. Treatment with single dose BTX-A into submandibular glands. Total dosage: 40 u if 15–25 kg 50 u if >25 kg	Saliva secretion Quality of life questionnaire	Maximal salivary flow rate of sublingual and submandibular glands reduced by 51–63%	16 week study period: 1 child did not drool, the 2nd had reduced drooling, the 3rd had decreased drooling initially but not sustained Conclusion: duration of effect variable	4
Jongerius <i>et al</i> (2004) ²	45 children (3–18 years) CP and severe drooling	Controlled, open label, clinical trial. Treatment with scopolamine patches, then with BTX-A into submandibular glands. Total dosage: 30 u if <15 kg 40 u if 15–25 kg 50 u if >25 kg	Saliva secretion (measured by DQ drooling quotient, TDS teacher drooling scale and VAS visual analogue scale)	DQ: 53% responded to scopolamine and 64% responded to BTX-A at 2 weeks and 49% at 24 weeks TDS: 61.5% good responders 8 weeks post BTX-A and 36% at 24 weeks VAS: reduced drooling throughout study	71% patients experienced moderate–severe side effects with scopolamine With BTX-A only non-severe side effects	3B
Jongerius <i>et al</i> (2004) ³	45 children (3–18 years) CP and severe drooling	Controlled, open label, clinical trial. Treatment with scopolamine patches, then with BTX-A into submandibular glands. Total dosage: 30 u if <15 kg 40 u if 15–25 kg 50 u if >25 kg	Salivary flow rate	Submandibular flow rate decreased 25% with scopolamine and 42% 2 weeks after BTX-A Significant reduction with BTX-A compared with scopolamine at 4 and 8 weeks but between 8 and 16 weeks significance disappeared	Although BTX-A resulted in a greater reduction to submandibular flow than scopolamine overall 95% responded to scopolamine with significantly lower response rates to BTX-A (varying from 69% at 2 weeks to 49% at 24 weeks)	3B
Bothwell <i>et al</i> (2002) ⁴	9 children (4–17 years) severe drooling and moderate or severe retardation (6 had CP)	Case series. Single injection of BTX-A 10 u divided between parotid glands	Saliva secretion (measured using dental bibs and DQ) Caregiver rating scales	For saliva secretion 33% good responders, 22% moderate responders, 11% poor responders and 33% non-responders 55% of parents thought improvement at 4 weeks and 22% at 16 weeks	16 week study period. BTX-A not as successful compared with other therapies e.g. surgery, anticholinergic therapy	4
Suskind and Tilton (2002) ⁵	22 subjects (8–21 years) CP and significant drooling	Prospective, open label, dose escalation study. 2 groups: Group 1 (12 subjects): injection of 10, 20 or 30 u in escalating doses into submandibular glands Group 2 (10 subjects) injection of 30 u into submandibular glands and 20, 30 or 40 u into the parotid glands	Saliva secretion (measured using dental roll weights, DQ) Quality of life questionnaire Evaluation of swallowing	Submandibular gland only 33% response Submandibular and parotid glands 80% response from caretaker evaluation No adverse effects on swallowing	Varying length of response Results difficult to interpret as recycling of patients within groups and no comment on optimum dosage within groups	4
Savarese <i>et al</i> (2004) ⁶	21 patients (5–18 years) with CP and problematic drooling	Open label, non blinded, prospective study. 15 u BTX-A into each parotid gland	Saliva secretion (measured using VAS, number of bibs used/day, weight of dental rolls)	53% marked improvement in drooling, 21% moderate improvement, 15% slight improvement, 11% no response	79% parents said they would have their child undergo treatment again	4

Should bubble baths be avoided in children with urinary tract infections?

Report by
G Modgil, A Baverstock, Paediatric Specialist Registrars, Taunton & Somerset NHS Trust, Taunton, UK; gitamodgil@doctors.org.uk
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Bubble baths are common products used by parents. Medical professionals, from students to consultants, can be heard across clinics throughout the country, advising

parents to avoid the use of bubble bath to help prevent another urinary tract infection in their child.

In our simple survey we could not find any labels on bubble baths intended for children or babies that reinforced this advice. Are we, as general paediatricians, providing unsubstantiated advice to our patients and parents?

Structured clinical question

In a child [patient] does the avoidance of bubble bath [intervention] help to prevent urinary tract infections [outcome]?

Search strategy and outcome

Secondary sources: Cochrane, Clinical Evidence—none.

Primary sources: Medline 1965 to present (urinary tract infection) AND (bubble bath) OR (soap)—none; search of (bubble bath) OR (soap).