Official Journal of the European Paediatric Neurology Society

Original article

What could predict effectiveness of Botulinum Toxin to treat drooling: A search for evidence of discriminatory factors on the level of body functions or structures

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ARTICLE INFO

Article history:
Received 12 November 2010
Received in revised form
22 February 2011
Accepted 16 June 2011

Keywords:
Children
Cerebral palsy
Body function and structure
BoNT-A
Drooling
Therapy outcome

ABSTRACT

Background: The treatment of drooling is important to families that experience the daily impact and research to elucidate clinical factors that play a role in the outcome of drooling treatment should be encouraged.
Aim: To define clinical factors that influence therapy outcome of submandibular Botulinum Toxin (BoNT-A) injections for drooling.
Methods: Prospectively collected data of 128 children with cerebral palsy were evaluated; 80 spastic and 48 dyskinetic movement disorder, mostly Gross Motor Function Classification System III and higher; over 70% had an IQ <70. In addition, 23 fully ambulant children with exclusively intellectual disability were treated for drooling by ultrasound-guided injections of BoNT-A into the submandibular glands. Salivary flow rates and drooling quotients were measured at baseline and at 8 weeks after injection. Extensive information about the oral motor performance was gathered. Successful clinical response was defined as a 50% reduction of the baseline Drooling Quotient; 85 children were responsive to BoNT-A and 66 children unresponsive.
Results: Five nominated clinical factors that possibly could influence saliva reduction (head position, lip seal, voluntary control over the tongue, control of voluntary movement functions, and mental age) did not influence the responsiveness to BoNT-A.
Interpretation: Other variables need to be considered to predict the outcome of BoNT-A treatment. This article describes the first attempt to reveal the contribution of body functions and structures to the outcome of BoNT-A submandibular injections.

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doi:10.1016/j.ejpn.2011.06.002

1. Introduction

Earlier drooling treatment results showed that up to 30% of patients did not respond to submandibular injection of Botulinum Toxin Type A (BoNT-A) if response was defined as a 30% reduction of submandibular salivary flow in combination with a 50% reduction of the Drooling Quotient (DQ).[1,2] Given the number of non responders, further research necessitates to search for factors that cause therapy failure.

BoNT-A injections result in a substantial direct effect on submandibular flow (SF) and have an indirect effect on the saliva regulatory mechanisms. Hence, the therapy effect of submandibular BoNT-A injections might be influenced on the one hand by pharmacological properties (type of Botulinum Toxin, dilution, injected dosage, secondary antibody response, and pharmacokinetics in relation to brand) and on the other hand by clinical variables (e.g. gross motor functions, cerebral palsy (CP) subtype, oral motor functions, mental ability). The primary purpose of the present cohort study was to reveal body functions and structures (as defined by the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY)) that could influence therapy outcome.

The majority of individuals with CP produce normal amounts of saliva, and it is generally accepted that the amount of saliva is not the decisive factor responsible for drooling in children with CP.[3] In the absence of evidence, researchers thus far have suggested a positive contribution to drooling severity of poor head control, dysfunctional oral motor control, a decreased swallow frequency, reduced intra-oral suction, dysarthria severity, and a degree of malocclusion in children with CP.[4–8] No correlation has been found between mobility level and the amount of saliva drooled.[5] Yet, little is known about clinical factors in relation to treatment outcome of submandibular gland BoNT-A application to treat drooling. Controlled data are not available, and it is unclear why some children with CP or developmental delay who drool respond well to BoNT-A while others only respond to a lesser extent. To date only a few population studies focusing on behavior modification therapy for drooling reduction have included clinical factors. It has been shown that saliva control and consequently drooling severity is most positively associated with age and the ability to swallow, control the head, and walk without aid.[9] Currently, there is no agreement about what child characteristics will distinguish between a "successful" or "unsuccessful" therapy response after submandibular BoNT-A injections.

This article describes the first attempt to reveal the contribution of body functions and structures to the outcome of BoNT-A submandibular injections to treat drooling. Body function and structure items, assumed as relevant clinical factors that might contribute to the treatment outcome are listed in Table 1. Given the costs of BoNT-A and the fact that anesthesia is needed, it is important to know what factors might influence treatment outcome of BoNT-A injections and to formulate strict indications for this therapy.

Table 1 – Definition of the clinical factors.

Variables	Definition
Head position	Ante flexion vs. lateral flexion-retro flexion-normal
Tongue protrusion	Permanently-often vs. sometimes-never
Lip seal in daily activity	Impossible-clearly different vs. slightly divergent-normal
Voluntary tongue control	No-almost never vs. sometimes-normal
Developmental Age	<4 years and 4–6 years with IQ <70 vs. 4–6 years with IQ >70 and >6 years
Control of voluntary movement functions	GMFCS I–III (ambulatory) vs. IV–V (non-ambulatory)
TOM-Dysarthria	Very serious-serious vs. moderate-mild-no dysarthria
DSS-Dysphagia	Very serious-serious vs. moderate-mild-minimal-no dysphagia

vs. = versus. GMFCS = Gross Motor Classification Function System: I = performing gross motor skills including running and jumping but reduced speed, balance, and coordination, V = no means of independent mobility; TOM = Therapy Outcome Measure (Dutch and modified version of the subscales for dysarthria); DSS = Dysphagia Disorder Survey (Dutch version).

2. Method

2.1. Participants

Prospectively collected data from 151 children (mean age 10 years 10 months, SD 4 years 10 months) screened in the outpatient drooling clinic at the Radboud University Nijmegen Medical Centre, The Netherlands between February 2000 and March 2010 were evaluated. The children were categorized as having CP or intellectual disability based upon Developmental Age (DA).[10] The children with CP were classified according to the predominant motor type.[11] The severity of motor disturbances was assessed by the Gross Motor Function Classification System (GMFCS).[12] Most of the children with CP had a mobility score of III or higher on the GMFCS; more than 70% had an Intelligence Quotient (IQ) below 70. All children with intellectual disabilities were ambulant, and had an IQ below 70.

Inclusion criteria were a score of 3 or higher on the Teacher Drooling Scale (a 5-point scale to express the clinical severity and frequency of drooling; 5 = constantly wet and leaking saliva, 1 = no drooling).[9] None of the participants had undergone previous BoNT-A therapy or surgical procedures for saliva control. All medications to control drooling or influencing salivary secretion were stopped at least 3 months before the start of the study. This research was conducted in accordance with national and international ethical standards. The Regional Committee on Research Involving Human Subjects approved the study. Informed consent was obtained from the parents or caregivers of all children.

2.2. Exclusion

No limits were set with regard to the child's level of cognitive development. Children with an ataxic CP subtype, or the