2-duct ligation versus botulinum toxin for severe drooling in children with cerebral palsy

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The main objective of the study is to address the relative efficacy of botulinum toxin and 2-duct ligation in children with cerebral palsy, who suffer from severe drooling despite maximal conservative treatment.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and peripartum neurological conditions
Study type	Interventional

Summary

ID

NL-OMON37173

Source
ToetsingOnline

Brief title
2-duct ligation versus botulinum toxin for severe drooling

Condition

- Congenital and peripartum neurological conditions

Synonym
drooling, sialorrhea

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Johanna Kinderfonds;Stichting Rotterdams Kinderrevalidatie Fonds Adriaanstichting;Phelps Stichting voor Spastici

Intervention

Keyword: botulinum toxin, cerebral palsy, drooling, surgery

Outcome measures

Primary outcome

The primary outcome of the study is the extent of drooling. This is mainly assessed using the drooling quotient and a VAS-score. Both methods have been used significantly.

The drooling quotient is a validated tool to semi-objectively quantify the extent of drooling. During two ten-minute sessions, the absence or presence of new saliva on the lip is recorded every fifteen seconds. The first session is performed while resting, the second while a child is distracted. The drooling quotient is obtained by dividing the number of observed drooling episodes by 0.4. The resulting quotient reflects the relative time a person drools.

The VAS is recorded by parents or caretakes, to investigate therapy results as experienced in the home situation. Scales of exactly 10 cm without visible subdivisions are presented, on which the average degree of drooling severity during the 10 to 14 days before assessment is to be indicated. A mark at the left end represents severe drooling; a mark at the right end means no drooling.

Secondary outcome

Secondary outcomes are the extent of drooling, quality of life, complications, admission time and duration of the procedure.

Study description

Background summary

Drooling is a serious clinical issue, affecting approximately 10-37% of all children with cerebral palsy. Involuntary loss of saliva is associated with significant morbidity. Although various treatments have been developed, little evidence exists regarding the relative efficacy of these approaches. It is, however, clear that surgery is among the most effective interventions. Rerouting the duct of the submandibular gland from the front of the mouth to the base of the tongue (submandibular duct relocation) has been the most common surgical technique for the past 20 years. Although this procedure is effective and relatively safe, it requires a hospital admission of several days, including one night of observation on an intensive care unit. This procedure is therefore a 'last resort' for involuntary saliva loss in the UMC St Radboud.

The invasiveness of submandibular duct relocation has led to the rise of a less invasive operation for various forms of drooling. This procedure involves ligating or clipping the submandibular ducts rather than rerouting them. Case series have described this as an effective and safe technique. Its main advantage over other approaches are drastically reduced operative times and days of admission. The procedure is commonly performed in daycare surgery and does not require admission to an intensive care unit. Especially for these vulnerable children, the reduced operative morbidity is a tremendous advantage. Experience with this procedure in the UMC St Radboud is so favourable that we intend to use it extensively in the future.

The most important alternative to surgery are botulinum toxin injections into the salivary glands. This procedure is in broad use since the beginning in the millennium, and has been extensively studied in the UMC St Radboud (among other international academic centres). This treatment is minimally invasive, and is therefore a first-line treatment for patients that do not respond well to (or are not eligible for) conservative measures. The main disadvantage of botulinum toxin is the fact that its effects are by definition temporary. Children will therefore frequently have to undergo multiple repeated injections. The decision of whether a repeated intervention has to be in the form of another botulinum toxin injection, or a more permanent solution in the form of surgery, is therefore often difficult.

The introduction of duct ligation as a treatment for drooling has made this choice even more complex. The reduced morbidity of the procedure compared to submandibular duct relocation, could for instance mean that wider use of surgery (rather than repeated injection with botulinum toxin) is indicated. To date however, there is absolutely no comparative information regarding the relative effectiveness, duration and morbidity of botulinum toxin and 2-duct

ligation. It is important to address this gap in scientific knowledge, as the choice between these treatments will frequently occur in clinical practice. Good comparative information would allow further development of an optimal treatment protocol for this vulnerable group of children.

Study objective

The main objective of the study is to address the relative efficacy of botulinum toxin and 2-duct ligation in children with cerebral palsy, who suffer from severe drooling despite maximal conservative treatment.

Study design

The study is designed as a randomized controlled trial. Included patients are treated by (repeated) injection of botulinum toxin, or surgical ligation of the submandibular ducts (2-duct ligation).

Intervention

Participants in the study undergo either injection with botulinum toxin or 2-duct ligation. Both procedures are performed in daycare surgery.

A) 2-duct ligation
The patient is put under general anesthesia. The floor of the mouth is infiltrated with a lidocaine/adrenaline solution. The floor of the mouth is opened around the orifice of the submandibular duct, and the submandibular duct is dissected distally. When the submandibular duct has been dissected sufficiently, it is clipped with vascular clips on two positions approximately 1 cm apart. The procedure is repeated on the contralateral side, and the floor of the mouth is sutured.
Standard peri-operative medication consists of co-amoxiclav for 7 days, and diclofenac for analgesia.

B) Botulinum toxin
Using general anesthesia, 25U of botulinum toxin (Botox; Allergan, Nieuwegein, Netherlands), reconstituted with 0.9% sodium chloride solution, is injected bilaterally in the submandibular glands using a 25-G needle and a 1-mL syringe. On injection, each dose is fractionated and divided over minimally 3 sites in the gland using ultrasound guidance.

Study burden and risks

The study does not carry any specific risks. The treatments in the study are also performed routinely in regular clinical practice, and have a good record for safety. The follow-up protocol of the study is not associated with increased risks.

The additional burden of participation is relatively limited, and adds up to a total of 1.5 hrs (informed consent, additional follow-up two weeks after procedure).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

- Age 6 years or above
- Cerebral palsy or other non-progressive neurological disease
- Severe drooling (Drooling Frequency >=3; Drooling Severity >=2)
- Conservative treatment has not led to adequate reduction of droolng

- Informed consent
- Cognitive ability of parents is adequate to participate in the study, as judged by the researchers.
- Participants are motived to return for follow up after 2, 8 and 32 weeks.

Exclusion criteria

- Concurrent participation in other medical study
- Previous surgery or anatomical abnormalities that prohibit either application of botulinum toxin or surgery
- Concurrent other treatment for drooling
- Use of benzodiazepines
- Allergy to botulinum toxin or other contraindication for botulinumtoxin or surgery.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-04-2012
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	12-07-2011

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-03-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-06-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL26144.091.11