MERZ THERAPEUTICS

LIÈGE université

WORKSHOP – 11 & 12/05/2026

SIALORRHEA
CONCEPTS &TREATMENTS

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CHU de Liège

CONTENT

1 NOSOLOGY

ANATOMY
PATHOLOGY
SIGNS & SYMPTOMS
DIAGNOSISC & SCALES

2 TREATMENT

NOSOLOGY

ANATOMY & CLINICAL FEATURES

ANATOMY & PHYSIOLOGY

- MAIN SALIVARY GLANDS
  - Parotids (serous cells +++)
  - Sub-mandibular (mixed, serous cells + mucous)
  - Sub-lingual (mixed, muuous cell++)
- ACCESSORIES SALIVARY GLANDS:
  - Von ebner, blandin-nuhn, glosso-palantines, weber
  - (palate, tip of the tongue, etc.)

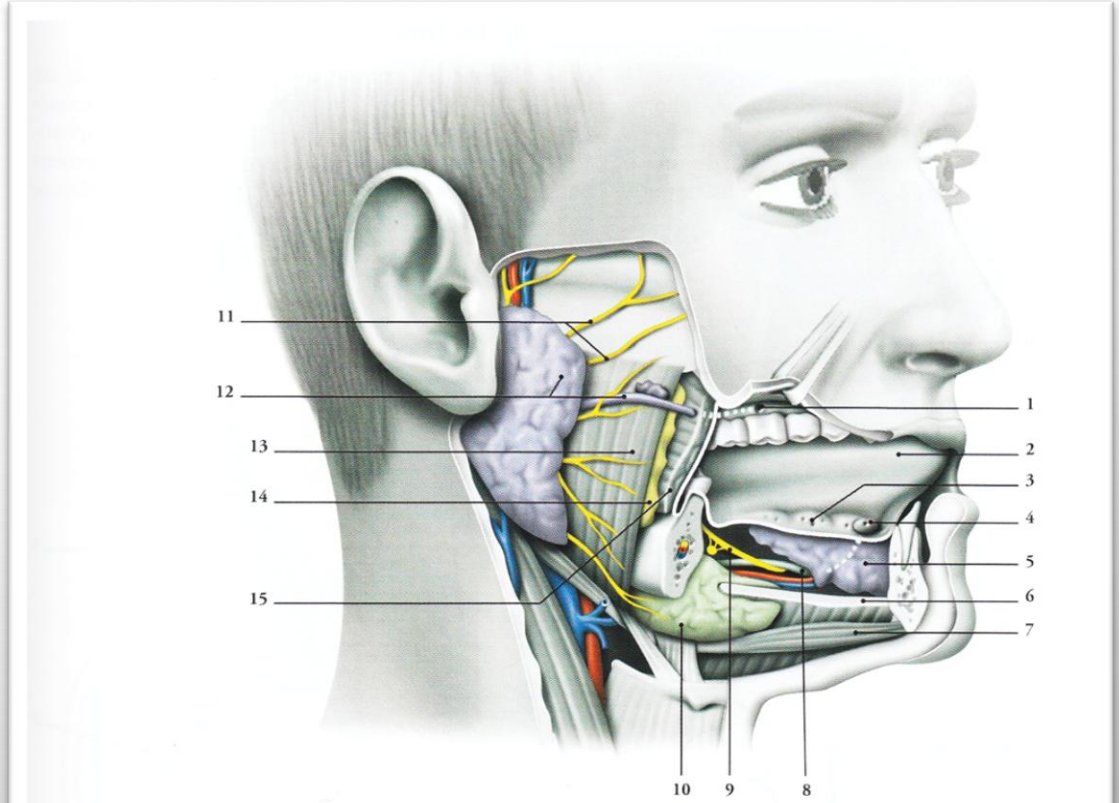
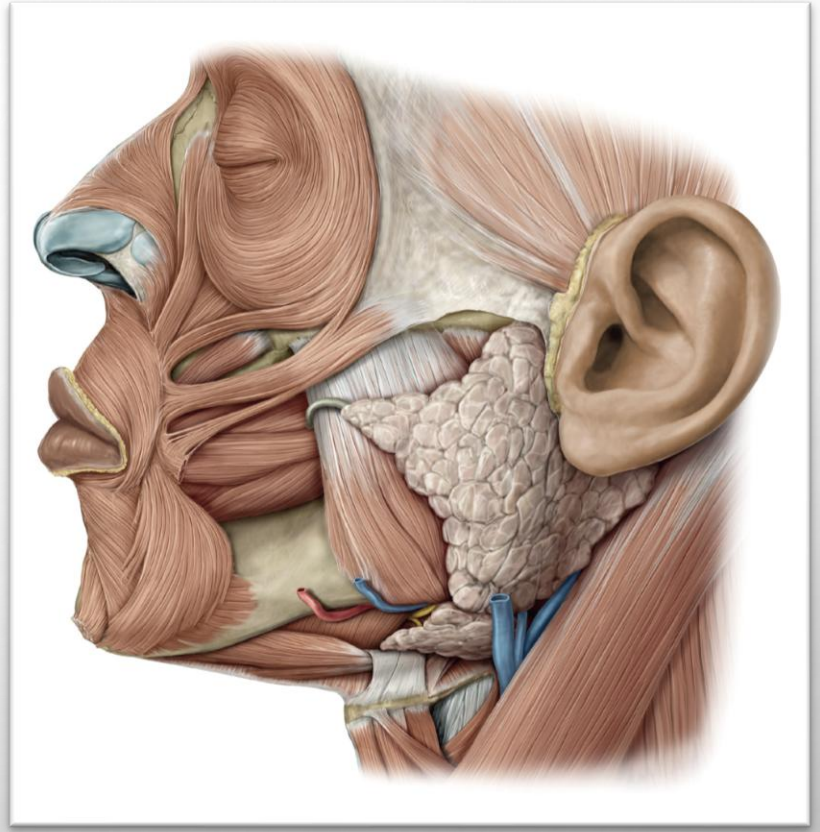


FIG. 21.1. Glandes salivaires

1. papille parotidienne
2. langue
3. caroncule sublinguale et ostiums des conduits sublinguaux
4. ostium du conduit submandibulaire
5. glande sublinguale
6. m. mylo-hyoïdien
7. m. digastrique
8. conduit submandibulaire
9. n. lingual et ganglion submandibulaire
10. glande submandibulaire
11. rameaux du n. facial
12. glande parotide et conduit parotidien
13. m. masséter
14. m. buccinateur
15. corps adipeux de la bouche

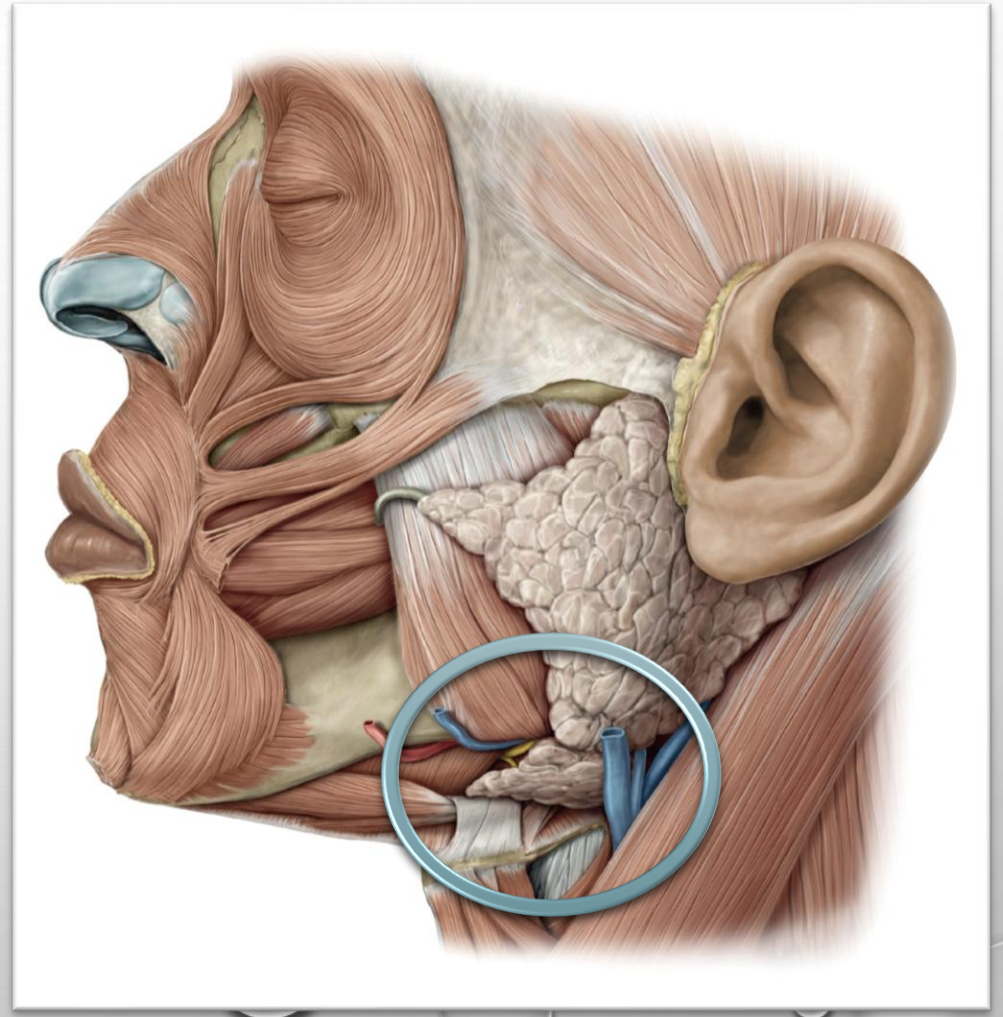
ANATOMY & PHYSIOLOGY

- PAROTID GLAND
  - Etymology: “around the ear”
  - In the parotid cavity
  - Weight: 25g
  - Excretory duct: Stenon’s duct
- POINT OF ATTENTION: FACIAL NERVE (LOW RISK)



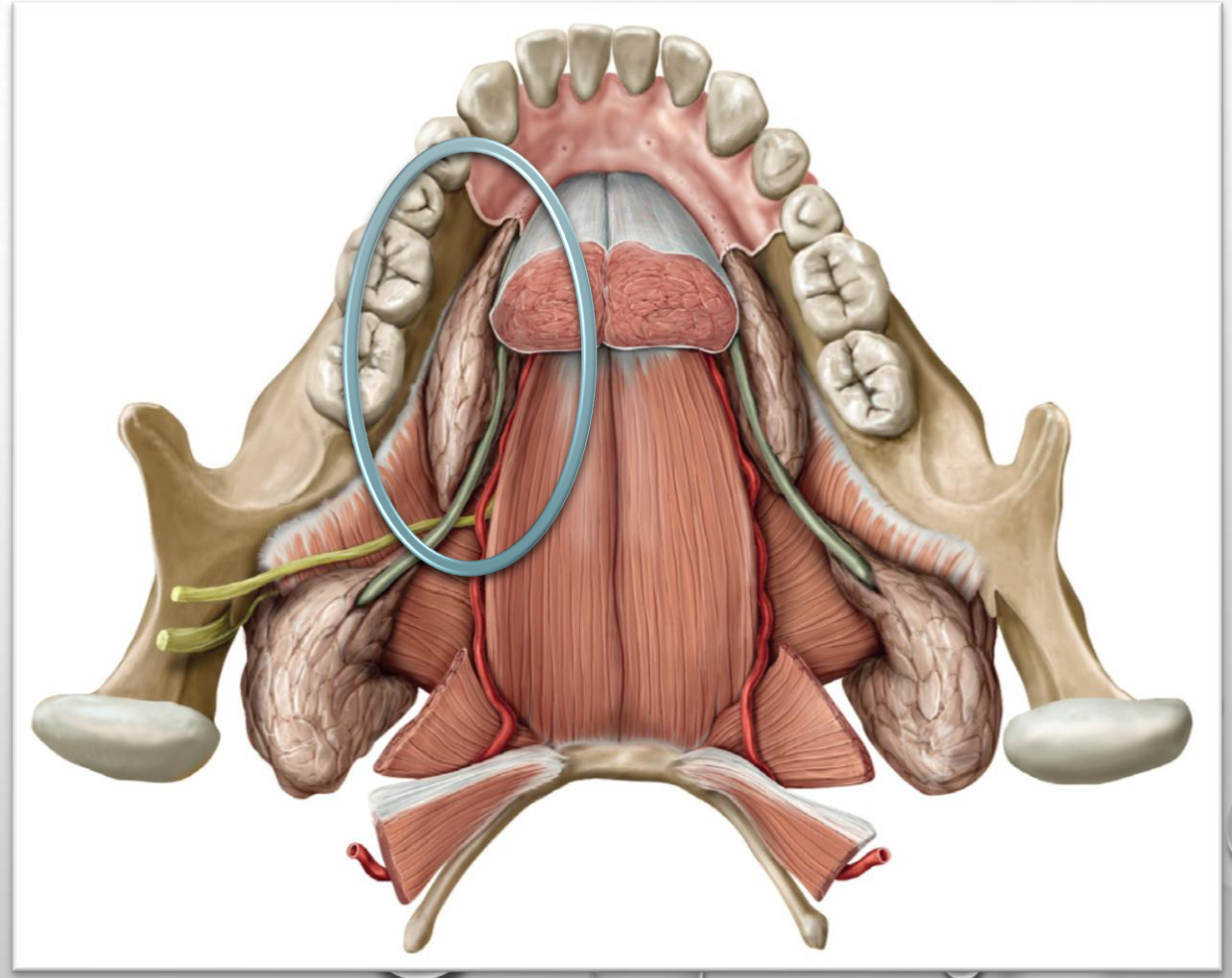
ANATOMIE & PHYSIOLOGIE

- SUB-MANDIBULAR GLAND
  - In the submandibular area
  - Weight : 7- 10g
  - Lots of inter-individual variations
- EXCRETORY DUCT: WHARTON'S DUCT



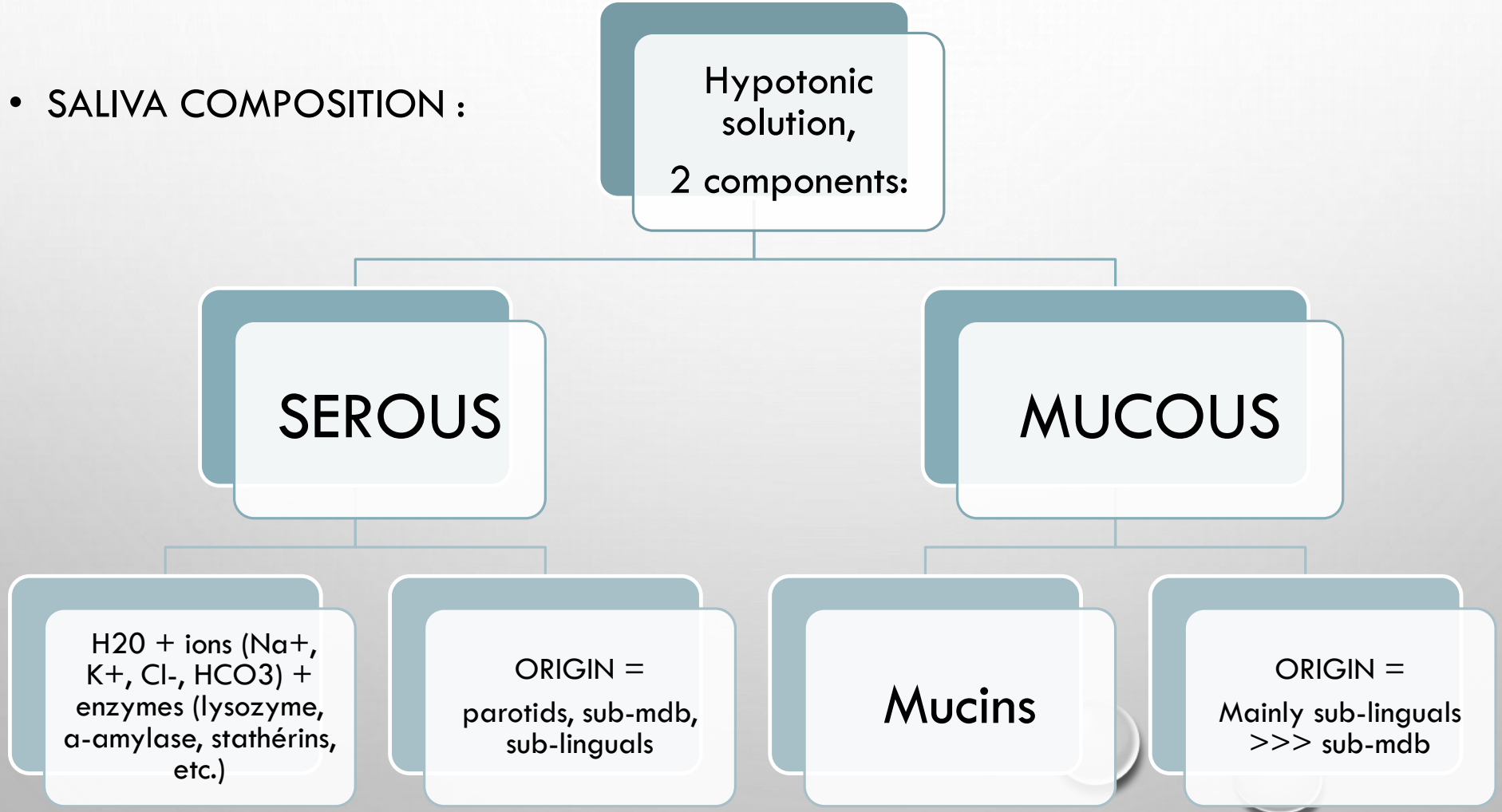
ANATOMIE & PHYSIOLOGIE

- SUB-LINGUAL GLAND
  - Agglomération of accessory glands
  - Several excretory ducts + Wharton's duct
- NON TARGETED WITH TOXIN



ANATOMY & PHYSIOLOGY

- SALIVA COMPOSITION :



ANATOMY & PHYSIOLOGY

- Composition of saliva:
  - Different Viscosity depending on the salivary gland :
    - Fluid for parotids
    - Thick for sub-mandibular glands
    - Even thicker for sub-linguals

ANATOMY & PHYSIOLOGY

- ROLE OF THE SALIVA
  - Preparation of the food bolus
  - Prevention of the caries
  - Prevention of xerostomia
  - Antibacterial role
  - Digestion
  - Gustative

ANATOMY & PHYSIOLOGY

- SALIVARY SECRETION
  - VOLUME: 2L per 24h
  - approx. 10 ml during sleep (8h)

- 50% = secretion at “rest”
- 50% = secretion in response to stimuli associated to oral intake

ANATOMY & PHYSIOLOGY

- ATTENTION:
  - Even if parotid glands are 3x bigger than sub-mandibular glands, they produce the same amount of saliva.
- CONTRIBUTION OF THE DIFFERENT SALIVARY GLANDS: VARIABLE
  - State of vigilance
  - Type of stimulation
  - Circadian rythm

ANATOMY & PHYSIOLOGY

Importance of accurate questions during the anamnesis

- CONTRIBUTION OF THE DIFFERENT SALIVARY GLANDS: VARIABLE

At rest (awake)	After gustative stim.	Asleep	Mechanical stim.
• Gld sub-mdb> 70% • Parotids: 20% • Sub-linguale + access.: 10%	• Gld sub-mdb: 45% • Parotids: 45% • Sub-linguale + access.: 10%	• Parotids: 0% • Gld sub-mdb: >45-80% • Gld access: variable	• Gld sub-mdb: 30% • Parotids: 60% • Sub-linguals + access.: 10%

Renaud BREHERET, Thèse de Médecine ORL, Angers, 2008

PATHOLOGY

- 2 DISTINCT CONCEPTS : HYPERSIALORRHEA VS PTYALISM
  - Ptyalism
    - Labial hypotonia
  - Salivary swallowing defect
    - Loss of automatic swallowing
    - Inefficient swallowing of saliva

Most frequent phenomenon implicated in neurological disorders

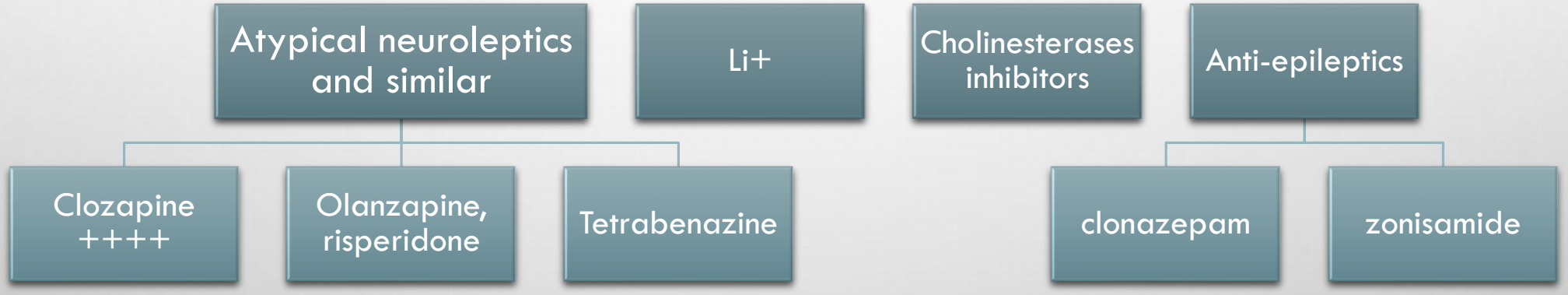
- HYPERSIALORRHEA:
  - Increase of salivary production, often responsible for salivary incontinence

PATHOLOGY

- NEUROLOGICAL CAUSES OR DISORDERS ASSOCIATED WITH SIALORRHEA/DYSPHAGIA
  - Parkinson's disease
  - Atypical parkinsonian syndroms
  - Stroke
  - Disorders with bulbar syndromes (ALS, myopathies, etc.)
  - Cerebral palsy (paediatrics)
  - Various dementia subtypes
  - Iatrogenous

PATHOLOGY

- NEUROLOGICAL CAUSES/DISORDERS ASSOCIATED WITH SIALORRHEA
  - IATROGENOUS



Unfortunately, these medications are mostly encountered in neurology, psychiatry, and particularly in Movement Disorders

PATHOLOGY

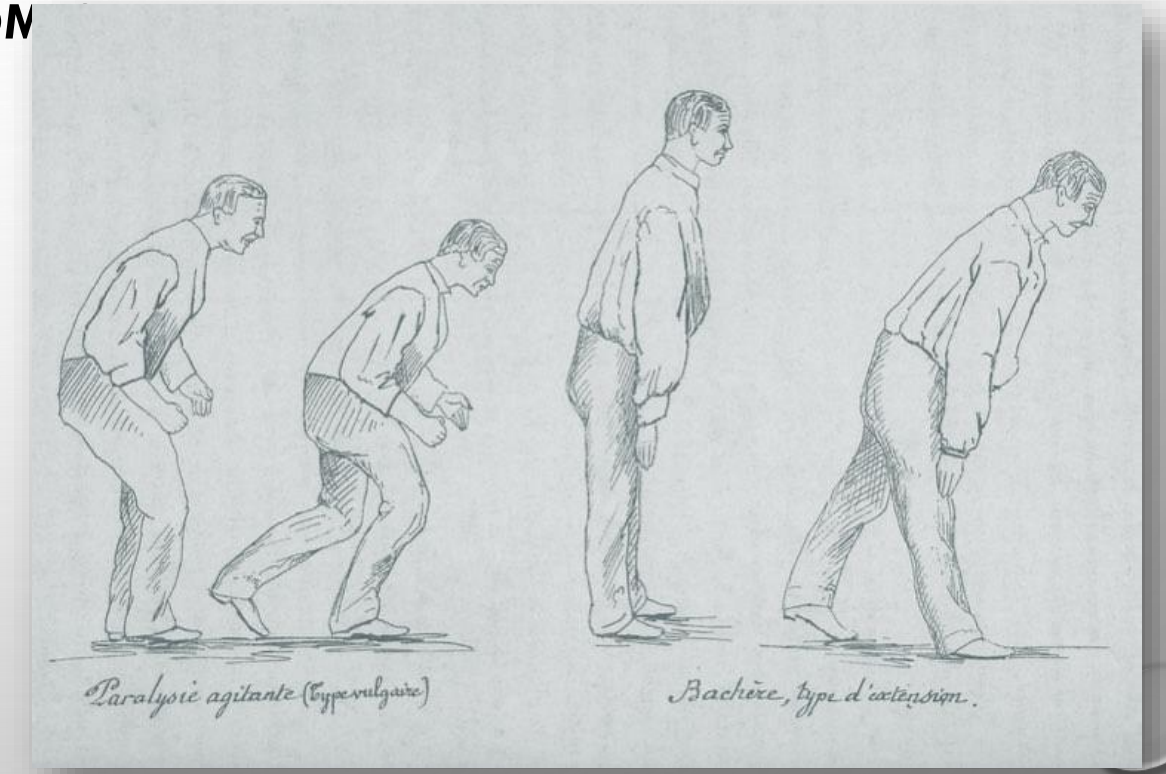
HYPERSIALORRHEA & ALS

- Epidemiology: 20-30% of the patients, at least
- No hyper-production
- CAUSES:
  - Labial continence defect
  - Postural abnormalities
  - Reduction of saliva draining (pharyngeal and lingual)
  - Inefficient cough
- Consequences
  - Drooling
  - Pharyngeal overload and saliva inhalation
  - Halitosis
  - Pneumopathies
  - Uncomfort
  - Social consequences

PATHOLOGY

HYPERSIALORRHEA & PARKINSONIAN SYNDROM

- EPIDEMIO: 40 TO 80% OF THE PATIENTS !!!
  - One of the most frequent of non-motor symptoms
  - This item is included in UPDRS part II
- MULTIPLE CAUSES
  - Saliva hyperproduction
  - Hypomimia and labial continence defect
  - Lingual Bradykinesia
  - Loss of automatic swallowing
  - Oro-pharyngeal dysphagia
  - Treatment: NL!



Charcot; Maladie de Parkinson

PATHOLOGY

HYPERSIALORRHEA & PARKINSONIAN SYNDROMES

- Worsened in OFF period
- Complaint: most of the time, concerns nocturnal hypersialorrhea or rest sialorrhea
- No real discomfort during meals

- MORE FREQUENT if the patient also presents cognitive decline
- MORE FREQUENT in certain subtypes (GBA, etc.)

PATHOLOGY

HYPERSIALORRHEA & STROKE

- PREVALENCE UNKNOWN: Depend on stroke subtype (facial involvement, brainstem stroke, etc.)
- MULTIPLES CAUSES:
  - Oral apraxia, impaired oral initiation of swallowing
  - Sensitive impairment in pharyngo-laryngeal region
  - Impaired consciousness (including the cases with nasogastric tube
  - Postural abnormalities
  - Loss or reduction of pharyngeal reflex in swallowing
  - Paresis of pharyngeal muscles, cerebellar syndrome, etc.

PATHOLOGY

HYPERSIALORRHEA & INTENSIVE CARE POLYNEUROPATHY

- Unknown prevalence
- However, high prevalence of dysphagia (up to 1/6 patients)

- CAUSES:
  - Impaired saliva swallowing
  - Associated neurological disorders or lesions
  - More frequent in case of associated cognitive impairment

- **<u>Reducing saliva production can help or hasten tracheotomie removal</u>**
  - But it can rarely prevent its introduction

PATHOLOGY

HYPERSIALORRHEA & ENT SURGERY (‼ NOT REIMBURSED ‼)

- ACUTE PHASE
  - Reduction of saliva in case of fistulae (pharyngostome) in post-operative period
  - Second intention treatment in cysts and saliva fistulae after parotidectomy

- LONG TERM
  - Cases of labial incontinence in various post-operative situations

PATHOLOGY

- OTHER NEUROLOGICAL CAUSES
  - CEREBRAL PALSY (CHILDREN)
  - CHOREA (Huntington disease, etc.)

- OTHER CAUSES (!!!! NOT REIMBURSED!!!!)
  - ENT NEOPLASIA, SURGERY, FISTULAE, ETC.

DIAGNOSIS & SCALES

- ANAMNESIS:
  - Ptyalism: permanent or at specific moments of the day?
  - Saliva: thin or thick?
  - Pharyngeous saliva stasis? Salivary inhalation?
- CONSEQUENCIES
  - INDIRECTS SIGNS: clothes, facial mask!, number of tissues used per day, etc.
  - Impact on speech fluency
  - Social impact

DIAGNOSIS & SCALES

- QUANTITATIVE APPROACH:
  - USFR
- QUALITATIVE APPROACH:
  - DSFS: "Drooling severity and frequency scale"

SEVERITY	FREQUENCY
1 - Never drools, dry	1 – No drooling
2 – Mild-drooling, only lips wet	2 – Occasionally drools
3 – Moderate- drool reaches the lips and chin	3 – Frequently drools
4 – Severe- drool drips off chin & onto clothing	4 – Constant drooling
5 – Profuse- drooling off the body and onto objects (furniture, books)	

IMPORTANT FOR THE REIMBURSEMENT PROCESS!!!!!

DIAGNOSIS & SCALES

> Int J Pediatr Otorhinolaryngol. 2015 Aug;79(8):1201-5. doi: 10.1016/j.ijporl.2015.05.010. Epub 2015 May 18.

Drooling quantification: Correlation of different techniques

Parisa Rashnoo [1], Sam J Daniel [2]

Affiliations + expand

PMID: 26092552 DOI: 10.1016/j.ijporl.2015.05.010

More information…

Abstract

Objectives: The aim of this study is to evaluate the correlation of the Drooling Quotient (DQ) score with the questionnaire-based Drooling Severity and Frequency Scale (DSFS) and the number of bib changes in a day. It is hypothesized that there is a significant positive correlation between these methods of assessment.

CONTENT

1 NOSOLOGY

2 TREATMENT

INTRO: BOTULINUM TOXIN
SIAXI STUDY
REIMBURSMENT
VIDEOS

TREATMENT

TOXIN – PRACTICAL ASPECTS - STUDIES

SIALORRHEA TREATMENT

- SPEECH THERAPY
  - Labial incontinence
    - reinforcement of the lip strap
  - Lack of oral initiation of swallowing, impairement in the pharyngeal reflex
    - Oral Stimulations
    - Motor oral therapy
  - Impairement in the swallowinf efficacy
    - strengthening of the tongue and the pharynx
    - Electrical stimulation (ongoing validation)

SIALORRHEA TREATMENT

- MEDICATIONS: ANTICHOLINERGICS
  - Variable choice, depending on local reimbursement conditions (scopoderm, etc.)
  - Patient with parkisonian features: Artane, small dosage?
  - Atropine (collyrium)
  - Glycopyrronium
  - Limitations: side effects!!! (In particular with cognitive impairment)

SIALORRHEA TREATMENT

- MEDICAL TREATMENT: GLYCOPYRRONIUM
  - To be prepared by the pharmacist

- Or Sialanar syrup
  - 312µg/mL
  - 250 mL
  - 5 mL, x3/ a day
  - (Approx. 413 euros)

Glycopyrronium syrup – preparation
Rp/ 0,5mg/ml in 100ml
dt/ 1 vial of 100 ml
Sp/ 3x a day: 2,5 mL (tsp)
(approx. 750 euros)

SIALORRHEA TREATMENT

- MEDICAL TREATMENT: ALTERNATIVE = ATROPINE
  - Not mentioned in the reimbursement rules
  - Collyrium

collyrium Atropine 1%
1 to 2 drops, 3x/ a day

SIALORRHEA TREATMENT

- SURGICAL TREATMENT
  - Rare
  - Excision of salivary glar
- RADIATION THERAPY TAR
  - 20 G in 4 sessions
  - 1 study in ALS (Pradat
  - 90% response +

> Int J Radiat Oncol Biol Phys. 2014 Mar 1;88(3):589-95. doi: 10.1016/j.ijrobp.2013.11.230. Epub 2014 Jan 7.

Radiation therapy for hypersalivation: a prospective study in 50 amyotrophic lateral sclerosis patients

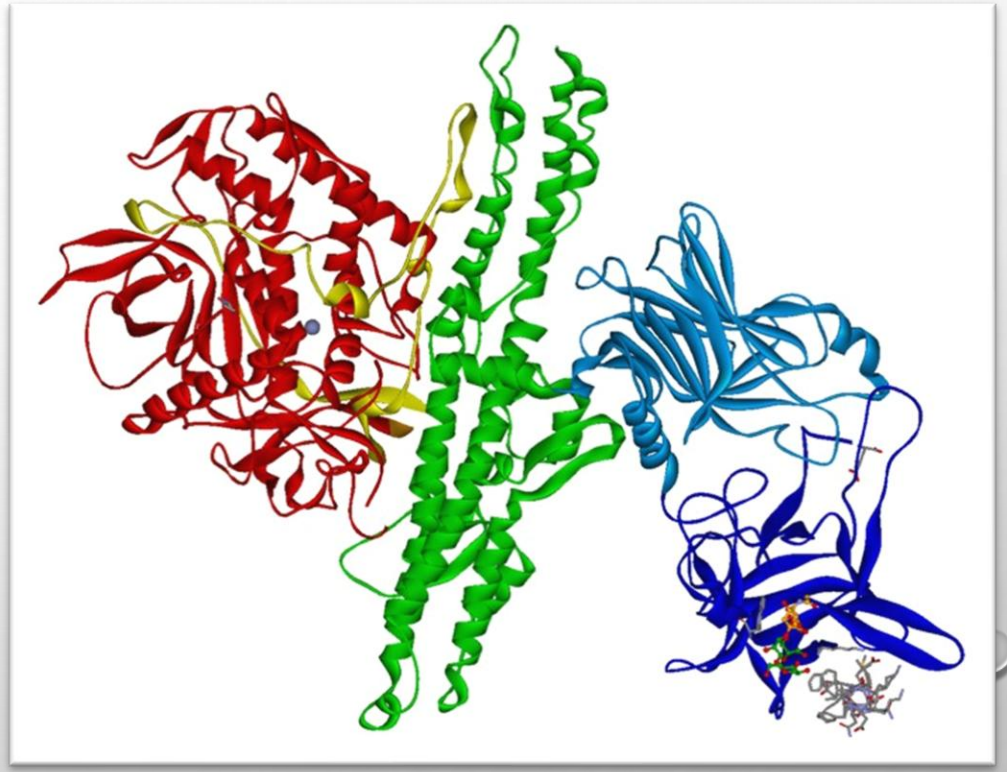
Avi Assouline [1], Antonin Levy [2], Maya Abdelnour-Mallet [3], Jesus Gonzalez-Bermejo [4], Timothée Lenglet [5], Nadine Le Forestier [6], François Salachas [5], Gaelle Bruneteau [5], Vincent Meininger [5], Sylvie Delanian [7], Pierre-François Pradat [8]

Affiliations + expand

PMID: 24411632 DOI: 10.1016/j.ijrobp.2013.11.230

BOTULINUM TOXIN

- BOTULINUM TOXIN TYPE A
- Voluminous molecule, PROTEINE (neurotoxine) – COMPLEX of 150 kda
- Stabilised by hemagglutinin nucleus in certain formula (NT of 150 kda + HA =900 kda)
- 3 brands available on the Belgian market (with a slightly different formula)
  - Xeomeen
  - Botox
  - Dysport



BOTULINUM TOXIN

- XEOMEEN: INCOBOTULINUM TOXIN A
- Powder – dilution necessary for its use
  - Rules and precautions!
- Dilution: NaCl, 2ml/100 U
- Vials of 50 U, 100 U et 200 U (Xeomeen ®)
- Collect the diluted product with a graduated syringe (1mL, is possible, to guarantee accuracy)

PART 2: THERAPEUTICS

DILUTION PROCESS

- PRACTICAL DEMONSTRATION

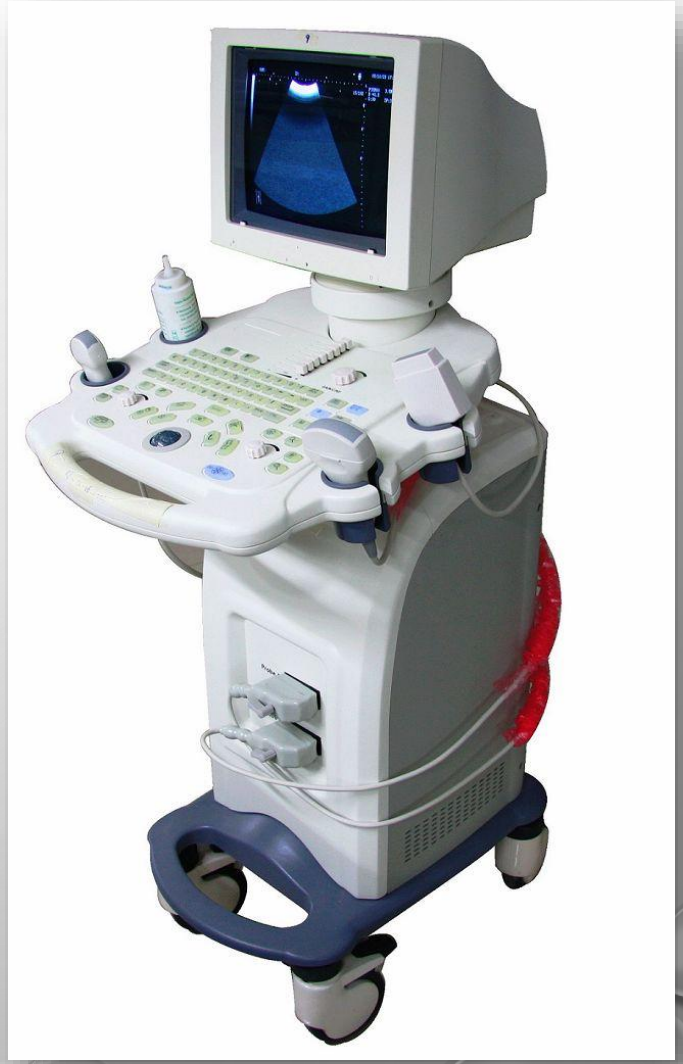
BOTULINUM TOXIN

INJECTION TECHNIQUE

- After reconstitution of the product, it must be stored inside an appropriate syringe (1 mL) with an appropriate needle (depending on the region which is going to be treated), for intramuscular injection
  - Salivary glands: blue or orange needle

GUIDANCE

- Ideally: ultrasound
- Some physicians only use anatomical landmarks



BOTULINUM TOXIN

Video Article

Ultrasound-guided Botulinum Toxin-A Injections: A Method of Treating Sialorrhea

Pierangelo Barbero[1], Marco Busso[2], Carlo Alberto Artusi[1], Stefania De Mercanti[1], Marco Tinivella[3], Andrea Veltri[2], Luca Durelli[1], Marinella Clerico[1]

[1]Clinical and Biological Sciences Department, Neurology Unit, University of Torino, San Luigi Gonzaga Hospital

[2]Oncology Department, Radiology Unit, University of Torino, San Luigi Gonzaga Hospital

[3]Clinical and Biological Sciences Department, Dietologic and Nutrition Unit, University of Torino, San Luigi Gonzaga Hospital

Correspondence to: Carlo Alberto Artusi at caartusi@gmail.com

URL: http://www.jove.com/video/54606
DOI: doi:10.3791/54606

Keywords: Medicine, Issue 117, botulinum toxin-A, ultrasound, ultrasound-guided injections, sialorrhea, dysphagia, drooling, neurological diseases

Date Published: 11/9/2016

Citation: Barbero, P., Busso, M., Artusi, C.A., De Mercanti, S., Tinivella, M., Veltri, A., Durelli, L., Clerico, M. Ultrasound-guided Botulinum Toxin-A Injections: A Method of Treating Sialorrhea. *J. Vis. Exp.* (117), e54606, doi:10.3791/54606 (2016).

Abstract

Neurological diseases can be complicated by sialorrhea, an excessive flow of saliva. Patients suffering from moderate to severe sialorrhea have an impaired quality of life, often worsened by correlated complications such as aspiration pneumonia, oral infections, dental caries, and

PART 2: THERAPEUTICS

PMID: 27911406

BOTULINUM TOXIN

J Neurol Neurosurg Psychiatry 2001;**70**:538–540

Treatment of sialorrhoea with ultrasound guided botulinum toxin type A injection in patients with neurological disorders

M Porta, M Gamba, G Bertacchi, P Vaj

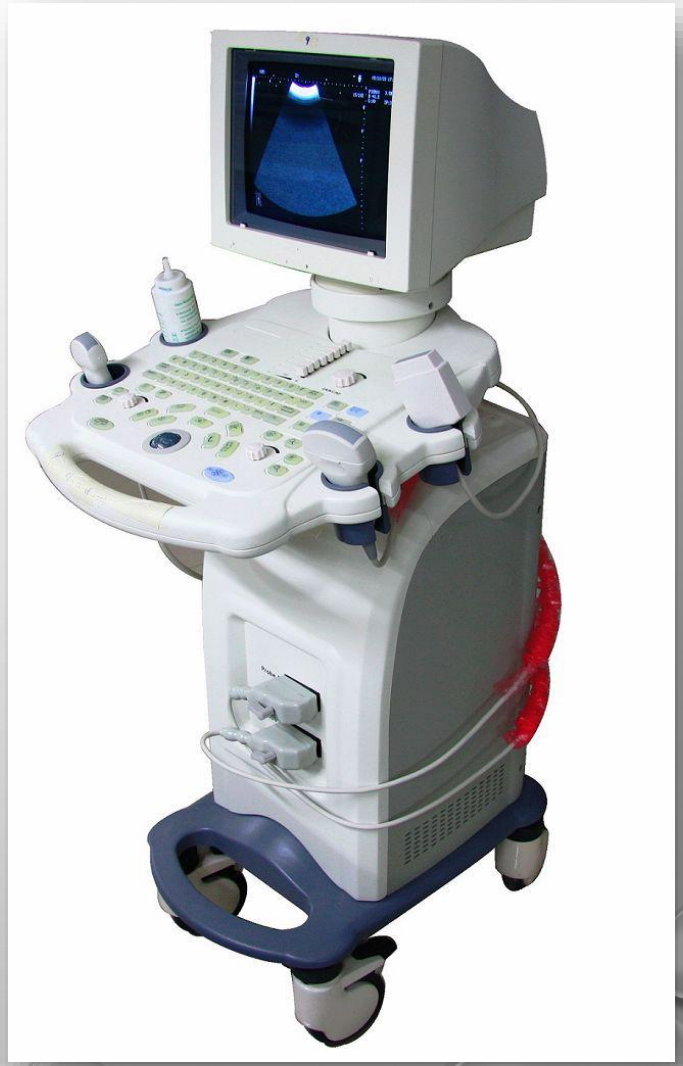
Abstract

***Objectives*—To investigate the safety and efficacy of ultrasound guided botulinum toxin type A (BTX-A) injections into salivary glands for the treatment of sialorrhoea in patients with neurological disorders.**

***Methods*—The parotid and submandibular glands of 10 patients were injected with BTX-A using ultrasound guidance. Before**

these include maceration of skin around the mouth, chin, and neck, which may result in secondary bacterial infections. In addition, sialorrhoea can interfere with speech and feeding and thus contribute to embarrassing and disabling social problems, which result in a decrease in quality of life.

Salivary glands are controlled by the autonomic nervous system, mediated by adrenergic and cholinergic nerve endings, and are primarily



PART 2: THERAPEUTICS

PMID: 11254784

BOTULINUM TOXIN

ELSEVIER

Clinical Neurology and Neurosurgery

Volume 106, Issue 2, March 2004, Pages 93-96

Ultrasound-guided versus 'blind' intraparotid injections of botulinum toxin-A for the treatment of sialorrhoea in patients with Parkinson's disease

Okan Dogu [a], Demir Apaydin [b], Serhan Sevim [a], Derya Umit Talas [c], Mihriban Aral [a]

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https://doi.org/10.1016/j.clineuro.2003.10.012

PMID: 15003297

« Comparisons of each treatment group also showed that ultrasound guided injections were superior to blind injections for saliva reduction »

BOTULINUM TOXIN

GUIDANCE: ULTRASOUND

DON'T FORGET!

- Closeness of oral floor muscles (such as mylohyoid); risk: tongue paresis and swallowing difficulties

-Closeness of masticatory muscles such as masseter

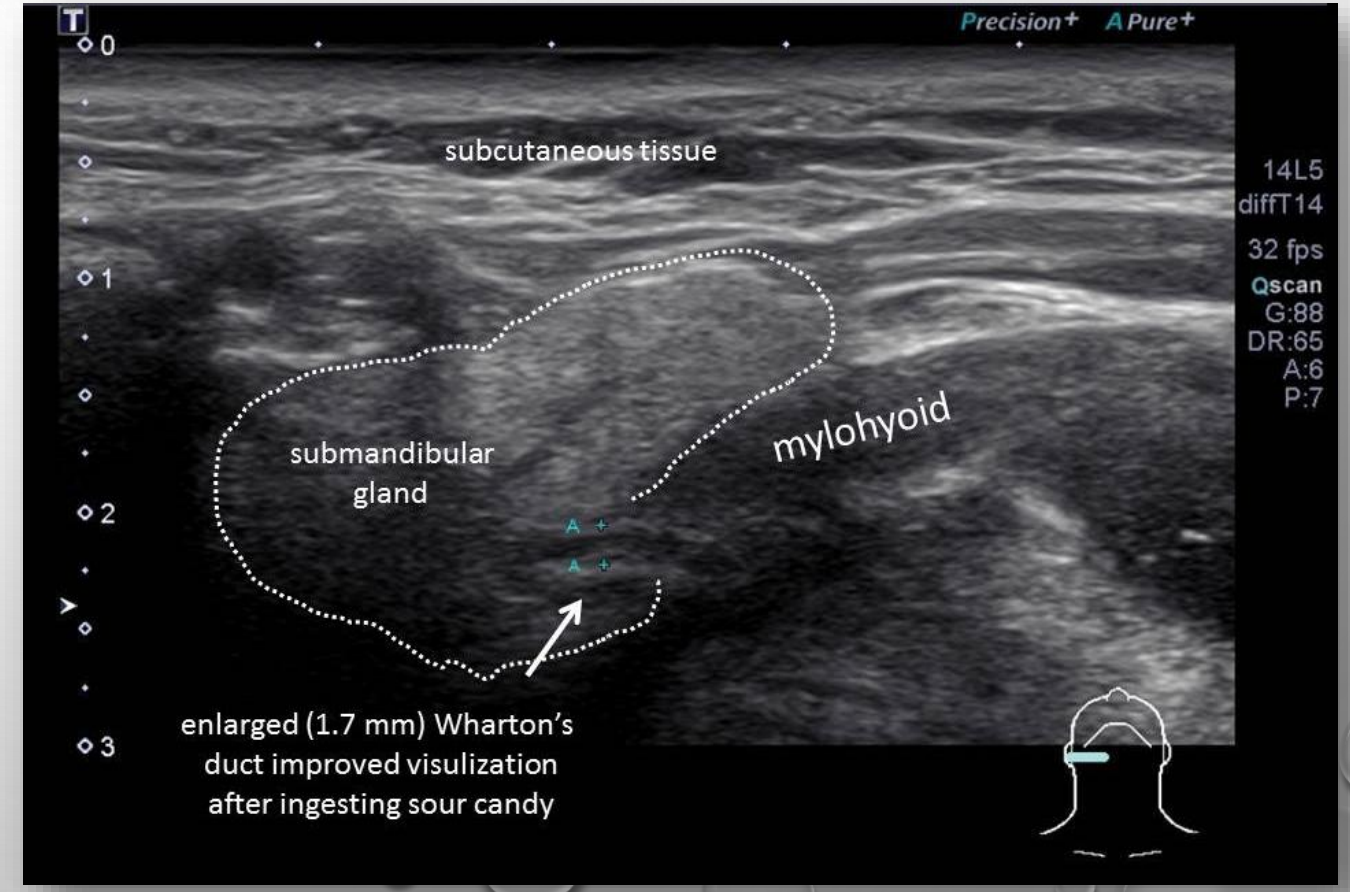

Image: Carver College of Medicine, Iowa

PART 2: THERAPEUTICS

VIDEO DEMONSTRATION

PART 2: THERAPEUTICS

VIDEO DEMONSTRATION

PART 2: THERAPEUTICS

VIDEO DEMONSTRATION

PART 2: THERAPEUTICS

EFFECTS

- TOXIN EFFECTS:
  - Saliva reduction (production)
  - BUT saliva is thicker

THEN, SALIVA IS NATURALLY VISCOUS AND SLIMY

Always ask the question to the patient and adjust next injection schedule if necessary

CONTRAINDICATION

- COMMON CONTRAINDICATIONS
  - Severe salivary stasis in pharynx
    - Inefficient swallowing
    - And/or inefficient cough
    - And/or sensibility reduction
    - And/or pharyngeal reflex reduction

! Be careful with position abnormalities associated with camptocormia !

POTENTIAL COMPLICATIONS

- Haematoma and post-injection pain
- Dry mouth and/or viscous saliva, which can be invalidating
- Diffusion of toxin (or inadequate injection) to
  - Buccal floor muscles
  - Masticatory muscles
  - Pharyngeal muscles => dysphagia
- Facial nerve lesion (very rare!)
  - (is the needle touches facial nerve's divisions inside parotid gland)

SIAXI STUDY

Randomized Controlled Trial > Neurology. 2019 Apr 23;92(17):e1982-e1991.
doi: 10.1212/WNL.0000000000007368. Epub 2019 Mar 27.

SIAXI: Placebo-controlled, randomized, double-blind study of incobotulinumtoxinA for sialorrhea

Wolfgang H Jost [1], Andrzej Friedman [2], Olaf Michel [2], Christian Oehlwein [2], Jaroslaw Slawek [2], Andrzej Bogucki [2], Stanislaw Ochudlo [2], Marta Banach [2], Fernando Pagan [2], Birgit Flatau-Baqué [2], János Csikós [2], Claire J Cairney [2], Andrew Blitzer [2]

Affiliations + expand

PMID: 30918101 PMCID: PMC6511076 DOI: 10.1212/WNL.0000000000007368
Free PMC article

Abstract

Objective: This pivotal phase III study, SIAXI, investigated the efficacy and safety of incobotulinumtoxinA for the treatment of chronic sialorrhea due to Parkinson disease (PD), atypical parkinsonism, stroke, or traumatic brain injury (TBI)

SIAXI STUDY

- PHASE III STUDY
  - Efficiency and safety of the botulinium toxin
  - Treatment of chronic sialorrhea
  - Parkinson disease, atypical parkinson-like syndromes, stroke, cranial trauma

  - Randomised, double-blinded study
  - 184 patients
  - Three arms: placebo (n=36), toxin 75 U (n=74), toxin 100 U (n=74)

SIAXI STUDY

- PHASE III STUDY
  - CHRONIC SALIVARY TROUBLES DUE TO MEUROLOGICAL DISEASE
    - Ongoing for more than 3 months
    - Score de drooling severity and frequency scale ≥ 6 pts; score ≥2 for each item
    - And score ≥ 3 pts for the item A concerning sialorrhea in the « modified radbout oral motor inventory for parkinson disease (« mromp »), score ≤ 2 et ≤3 respectively for the items a et c concerning swallowing function in the original romp

SEVERITY	FREQUENCY
1 - Never drools, dry	1 – No drooling
2 – Mild-drooling, only lips wet	2 – Occasionally drools
3 – Moderate- drool reaches the lips and chin	3 – Frequently drools
4 – Severe- drool drips off chin & onto clothing	4 – Constant drooling
5 – Profuse- drooling off the body and onto objects (furniture, books)	

SIAXI STUDY

- PHASE III STUDY
  - EXCLUSION CRITERIA:
    - Other causes of sialorrhea
    - Anti –secretory treatment within the 4 weeks before inclusion
    - Modifications in the treatments with impact on salivary secretion
    - Recurrent aspiration pneumopathies
    - Recent treatment with toxin (during the previous year for sialorrhea, or ans l'année pour weeks for other indications)
    - Hypersensibility to toxin
    - Surgery (anterior or scheduled) for sialorrhea

SIAXI STUDY

- EFFICIENCY ASSESSMENT
  - UNSTIMULATED SALIVARY FLOW RATE
    - Teeth brushed une heure avant le test, hours before the test
    - Then no eat, no smoke
    - Drink water 30 minutes before the test.

    - Direct collection of the saliva
    - Using 4 specific swabs (salimetrics oral swabs 2-ml capacity, salimetrics, carlsbad, CA)
    - Placed at the ostia of the salivary ducts during 5 minutes
    - Weighted before and after the test: the difference = salivary flow in g/min.
    - Re-test after 30 minutes, analysis of the mean values.

SIAXI STUDY

- EFFICIENCY ASSESSMENT
  - GLOBAL IMPRESSION OF CHANGE SCALE
    - Question asked to the patient and the caregiver
    - Likert scale with 7 points,
      - from (very much worse)to +3 (very much improved)
    - For patients: “Compared to how you were doing just before the last injection into your salivary gland, what is your overall impression of how you are functioning now as a result of this treatment?”
    - For caregivers: “Compared to how the patient was doing just before the last injection into his/her salivary gland, what is your overall impression of how he/she is functioning now as a result of this treatment?”

SIAXI STUDY

- EFFICACY ASSESSMENT
  - DSFS

SEVERITY	FREQUENCY
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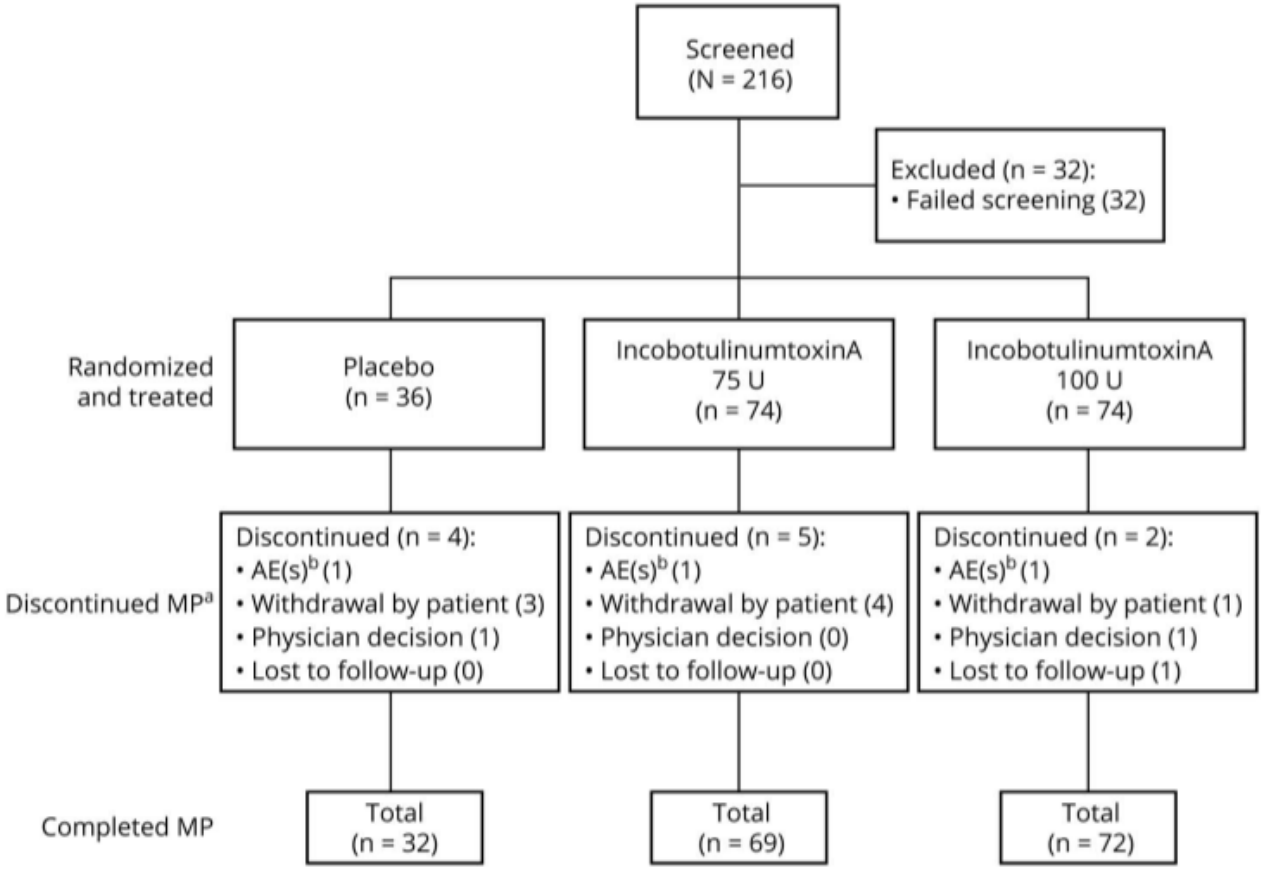
- ADVERSE EVENTS RECORDING

SIAXI STUDY

RESULTS



An AE leading to discontinuation occurring in one placebo patient was not considered a treatment-emergent AE (AE with onset or worsening at or after treatment). [a]Multiple reasons for withdrawal could be listed; [b]AEs were not treatment-related. AE = adverse event; MP = main period.

SIAXI STUDY

RESULTS

Table 1 Patient demographics and baseline characteristics

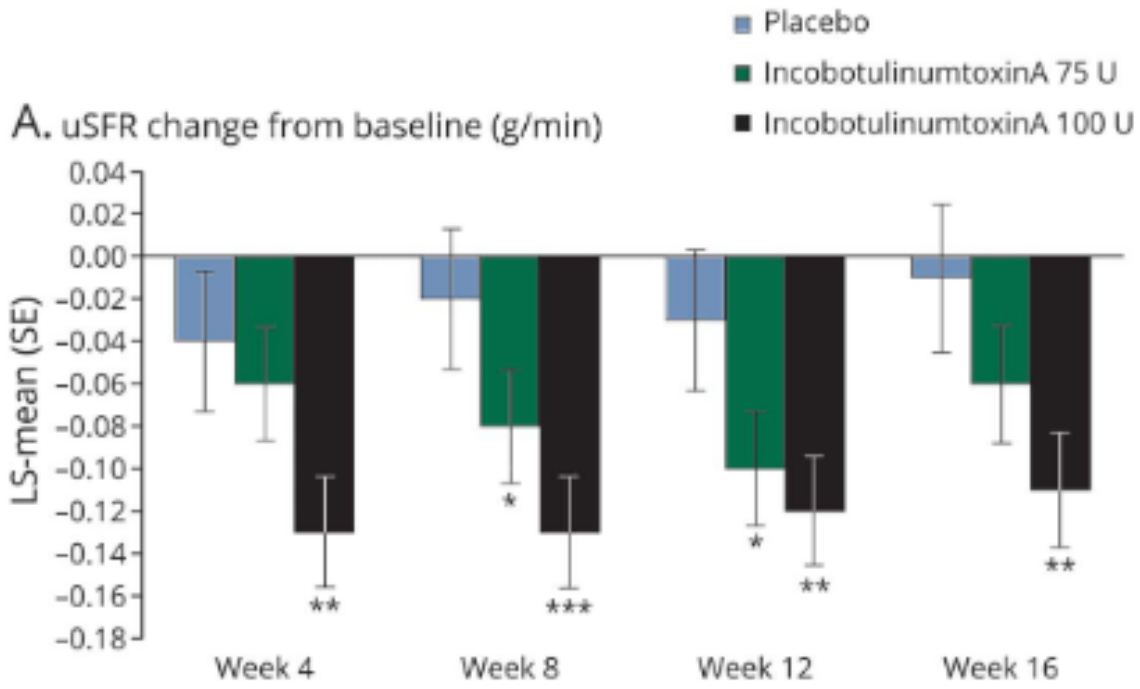
Characteristic	Placebo (n = 36)	IncobotulinumtoxinA 75 U (n = 74)	IncobotulinumtoxinA 100 U (n = 74)	Total (N = 184)
Sex, n (%)				
Male	28 (77.8)	50 (67.6)	52 (70.3)	130 (70.7)
Female	8 (22.2)	24 (32.4)	22 (29.7)	54 (29.3)
Age, y, mean (SD)	63.5 (10.6)	65.2 (11.7)	66.0 (11.6)	65.2 (11.4)
Weight, kg, mean (SD)	80.6 (16.4)	78.4 (17.1)	79.8 (14.0)	79.4 (15.7)
BMI, kg/m^2, mean (SD)	28.5 (6.0)	26.7 (5.2)	27.7 (3.8)	27.5 (4.9)
Drooling etiology, n (%)				
PD	26 (72.2)	51 (68.9)	53 (71.6)	130 (70.7)
Atypical parkinsonism	3 (8.3)	8 (10.8)	5 (6.8)	16 (8.7)
Stroke	6 (16.7)	13 (17.6)	14 (18.9)	33 (17.9)
Traumatic brain injury	1 (2.8)	2 (2.7)	2 (2.7)	5 (2.7)
UPDRS section III score, mean (SD) [n]	29.2 (12.7) [29]	33.1 (17.2) [59]	30.3 (15.1) [58]	31.2 (15.6) [146]
uSFR, g/min, mean (SD)	0.38 (0.23)	0.42 (0.28)	0.40 (0.27)	0.40 (0.26)
DSFS score, mean (SD)	6.97 (1.06)	6.88 (0.91)	6.78 (0.90)	6.86 (0.93)
Concomitant anti-PD medication, n (%)[a]				
Dopaminergic agents	28 (77.8)	57 (77.0)	58 (78.4)	143 (77.7)
Anticholinergic agents[b]	0 (0.0)	2 (2.7)	2 (2.7)	4 (2.2)
Injection guidance, n (%)				
Ultrasound-guided	18 (50.0)	45 (60.8)	41 (55.4)	104 (56.5)
Anatomical landmark–guided	18 (50.0)	29 (39.2)	33 (44.6)	80 (43.5)

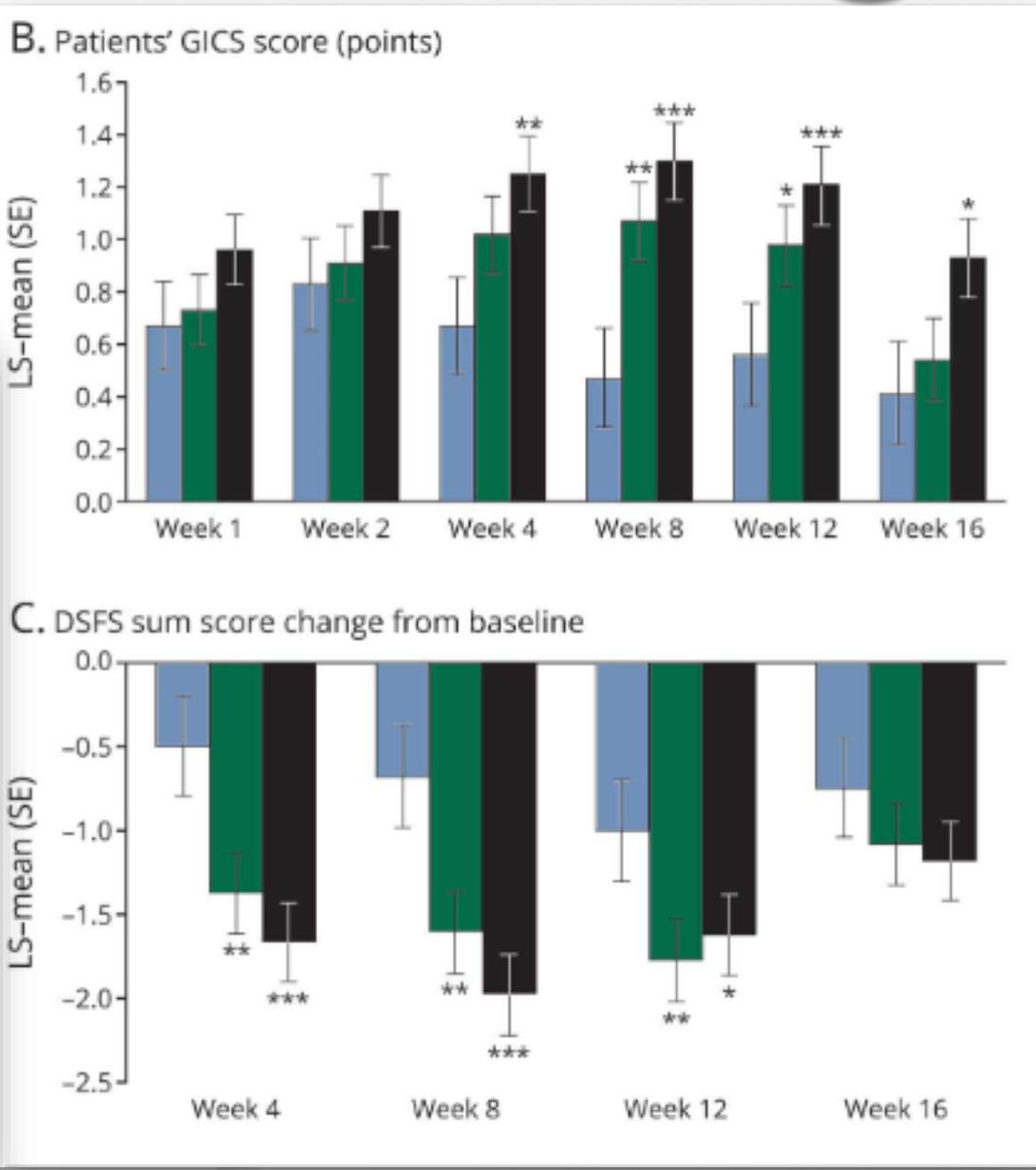
Abbreviations: BMI = body mass index; DSFS = Drooling Severity and Frequency Scale; PD = Parkinson disease; UPDRS section III = Unified Parkinson's Disease Rating Scale section III "motor examination" for patients with PD and atypical parkinsonism; uSFR = unstimulated salivary flow rate.
[a] Stable dose in patients with PD and atypical parkinsonism.
[b] Four patients were treated with biperiden during the main phase.

SIAXI STUDY

RESULTS

Figure 2 Clinical outcomes over time





SIAXI STUDY

ADVERSE EVENTS

Table 2 Summary of AEs

Patients	Placebo (n = 36)	IncobotulinumtoxinA, 75 U (n = 74)	IncobotulinumtoxinA, 100 U (n = 74)	Total incobotulinumtoxinA (N=148)
Any AE	15 (41.7)	32 (43.2)	34 (45.9)	66 (44.6)
Any treatment-related AE	3 (8.3)	7 (9.5)	6 (8.1)	13 (8.8)
Any AESI[a]	0 (0.0)	5 (6.8)	5 (6.8)	10 (6.8)
Any treatment-related AESI	0 (0.0)	3 (4.1)	1 (1.4)	4 (2.7)
Any SAE	3 (8.3)	6 (8.1)	9 (12.2)	15 (10.1)
Any treatment-related SAE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any AE leading to discontinuation[b]	0 (0.0)	1 (1.4)	1 (1.4)	2 (1.4)
Any treatment-related AE leading to discontinuation	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any fatal AE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any fatal treatment-related AE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Abbreviations: AE = adverse event; AESI = adverse event of special interest; SAE = severe adverse event.
Data represent number of patients, n (%). AEs in the main period were defined as AEs with onset or worsening after the first injection of incobotulinumtoxinA or placebo up to and before the first injection of the extension period.
[a] AESIs were classified based on a predefined list of AEs that could potentially indicate toxin spread (MedDRA version 19.1), regardless of whether an AE was regarded as treatment-related by the investigator. AESIs occurring in the incobotulinumtoxinA 75 U and 100 U groups, respectively, were as follows: dysphagia (n = 3 [2 related], n = 0); dry mouth (n = 0, n = 2 [1 related]); dysarthria (n = 0, n = 1); speech disorder (n = 1 [related], n = 0); dysphonia (n = 0, n = 2); bradycardia (n = 1, n = 0); and eyelid ptosis (n = 1 [related], n = 0). AEs describing dry mouth considered to be severe, serious, or irreversible were reported as AESIs.
[b] AEs leading to discontinuation were gastrointestinal obstruction and pneumonia of a severe intensity, not related to treatment.

SIAXI STUDY

- Level 1 evidence regarding the efficacy of botulinum toxin injection for the treatment of hypersialorrhea in adults
  - Effective treatment
  - Well tolerated
  - Positive effect for at least 16 weeks when using 100 U

AFTER THE SIAXI STUDY

Randomized Controlled Trial > Parkinsonism Relat Disord. 2020 Jan;70:23-30.
doi: 10.1016/j.parkreldis.2019.11.024. Epub 2019 Nov 26.

Long-term incobotulinumtoxinA treatment for chronic sialorrhea: Efficacy and safety over 64 weeks

Wolfgang H Jost [1], Andrzej Friedman [2], Olaf Michel [3], Christian Oehlwein [4], Jaroslaw Slawek [5], Andrzej Bogucki [6], Stanislaw Ochudlo [7], Marta Banach [8], Fernando Pagan [9], Birgit Flatau-Baqué [10], Ulrike Dorsch [11], János Csikós [12], Andrew Blitzer [13]

Affiliations + expand

PMID: 31794936 DOI: 10.1016/j.parkreldis.2019.11.024

Free article

Abstract

Background: Botulinum neurotoxin (BoNT) is an effective treatment for chronic sialorrhea; however, reliable and robust evidence supporting long-term efficacy and safety is lacking. This study investigated the efficacy and safety of repeated incobotulinumtoxinA injections for chronic sialorrhea over 64 weeks.

REIMBURSMENT: CRITERIA

- Mrs Caroline De Winter has initially prepared this section
- These criteria are quite complex and the registering must be done via ehealth platform (and the tedious CIVARS process)

XEOMEEN FOR SIALORRHEA

REIMBURSMENT

Caroline De Winter
Key Account Manager BeLux
Merz Therapeutics

WHICH PATIENTS ARE ELIGIBLE FOR THE REIMBURSMENT?

- Adults (18 years old at least)
- moderate to severe sialorrhea
  DSFS score: at least 6
- Chronic sialorrhea: at least 3 months
- **Sialorrhea due to any neurological disorder**
- Therapeutic failure with glycopyrronium
  Treated at least once
  Insufficient control of the symptoms
  Too many side effects

HOW TO DEFINE « MODERATE TO SEVERE » SIALORRHEA?

DROOLING SEVERITY AND FREQUENCY SCALE (DSFS) SCORE: MINIMUM 6

SEVERITY	FREQUENCY
1 - Never drools, dry	1 – No drooling
2 – Mild-drooling, only lips wet	2 – Occasionally drools
3 – Moderate- drool reaches the lips and chin	3 – Frequently drools
4 – Severe- drool drips off chin & onto clothing	4 – Constant drooling
5 – Profuse- drooling off the body and onto objects (furniture, books)	

DROOLING SEVERITY (DS)
SCORE: MINIMUM 2

DROOLING FREQUENCY (DF)
SCORE: MINIMUM 2

INITIAL TREATMENT

- **1rst treatment session: reimbursed**

100 U:
2 vials of 50 U
1 vial of 100 U

- **Assessment 4 to 8 weeks after the injection**

!!!

uSFR
GICS
Comfort

GLOBAL IMPRESSION OF CHANGE SCALE

GICS score:

How do you estimate patient's sialorrhea now when compared to the situation just before the last injection in salivary glands?

-3	-2	-1	0	+1	+2	+3
	much worse		unchanged		much better	
very much worse		worse		better		very much better

EXTENSION ONCE A YEAR

- **EFFICACITY SHOULD BE DEMONSTRATED AFTER INITIAL TREATMENT**

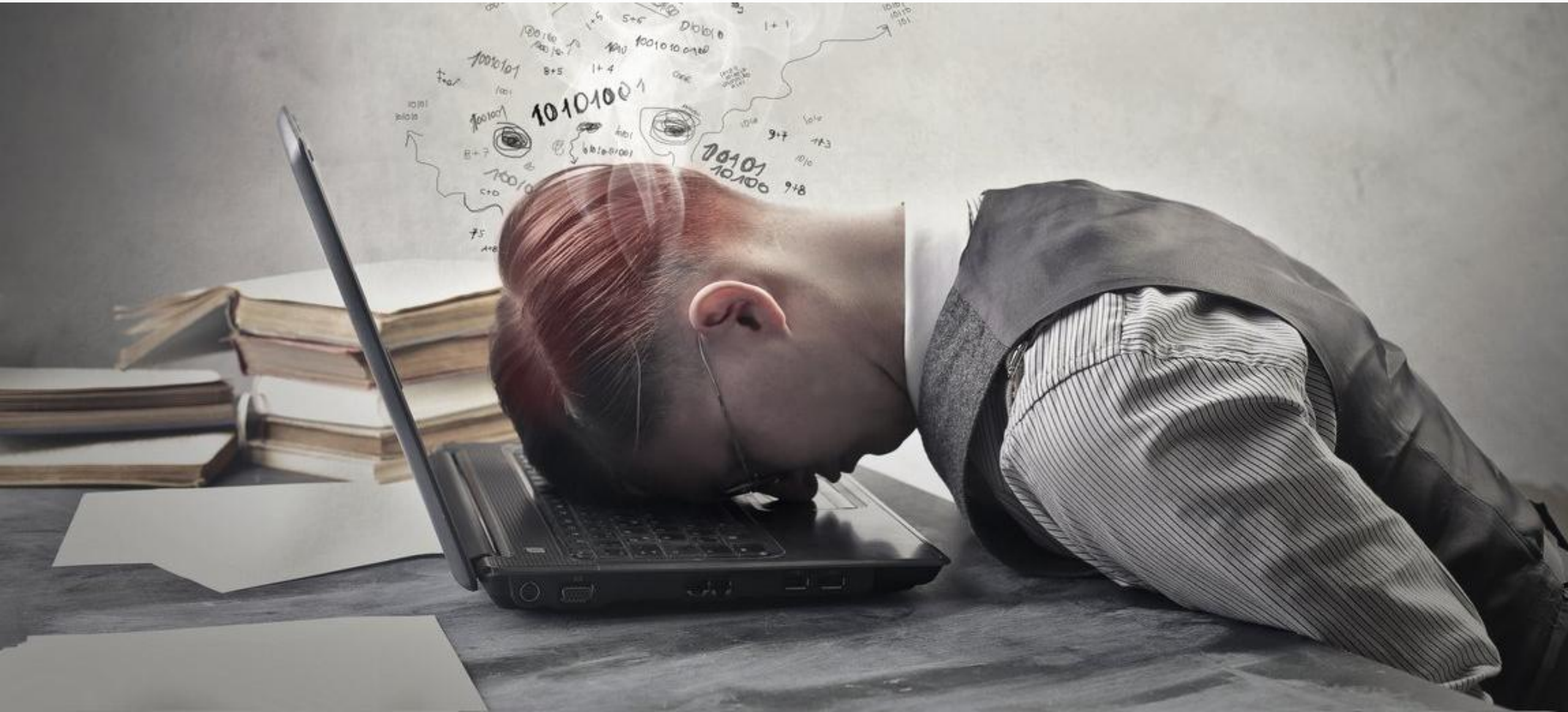
  GICS SCORE: MINIMUM +1

- **AFTER THE AUTHORIZATION:**
  A period of maximum 12 months is reimbursed, corresponding to maximum 4 treatment sessions

  400 UNITS IN TOTAL:

  8 VIALS OF 50 UNITS OR
  4 VIALS OF 100 UNITS OR
  ANY COMBINATION

A FEW “SIMPLE” STAGES…



XEOMEEN reimbursement checklist

to treat chronic sialorrhea in neurological disorders

MERZ THERAPEUTICS

Physician's name:

Patient's name:

Date of first XEOMEEN injection:

Date of GICS score:

Reimbursement can be requested via eHealth by specialists in physical medicine and rehabilitation, neurology or otorhinolaryngology.

Step 1: Glycopyrronium

☐ Check the box if glycopyrronium treatment is partly/not effective or if it causes side effects.

Step 2: DSFS score (Drooling Severity and Frequency Scale score)

Write down the DS score, the DF score and the DSFS sum score below. Check the appropriate box for every minimum score reached.

Drooling	Points
Severity	
Dry-never drools,	1
Mild-only lips wet	2
Moderate-drool reaches the lips and chin	3
Severe-drool drips off chin and onto clothing	4
Profuse-drooling off the body and onto objects (furniture, books)	5

Drooling	Points
Frequency	
Never drools	1
Occasionally drools	2
Frequently drools	3
Constantly drools	4

Drooling Severity (DS) score	
☐ ≥ = 2:	

Drooling Frequency (DF) score	
☐ ≥ = 2:	

DSFS sum score (DS score + DF score)	
☐ ≥ = 6:	0

Have you been able to check all 4 boxes in step 1 and 2? Then XEOMEEN is reimbursed to treat this patient.

Step 3: GICS score (Global Impression of Change Scale score)

4 to 8 weeks after first XEOMEEN treatment, an improvement should be observerd for further reimbursement. Use the GICS score by answering the following question and checking the appropriate box: Compared to how the patient was doing just before the last injection into the salivary glands, what is the overall impression of how the patient is functioning now as a result of this treatment?

-3	-2	-1	0	+1	+2	+3
☐	☐	☐	☐	☐	☐	☐
very much worse	much worse	worse	unchanged	better	much better	very much better

Is the GICS score at least +1? Then XEOMEEN reimbursement is extended by 12 months at a maximum of 400 units for 4 treatments. Step 3 can be repeated for new 12 months extensions.

PQC BEEN 3412 APR 22

CHECKLIST STAGE 1: GLYCOPYRRONIUM

Step 1: Glycopyrronium

☐ Check the box if glycopyrronium treatment is partly/not effective or if it causes side effects.

CHECKLIST STAGE 2: DSFS SCORE

Step 2: DSFS score (Drooling Severity and Frequency Scale score)

Write down the DS score, the DF score and the DSFS sum score below. Check the appropriate box for every minimum score reached.

Drooling	Points
Severity	
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Profuse-drooling off the body and onto objects (furniture, books)	5

Drooling	Points
Frequency	
Never drools	1
Occasionally drools	2
Frequently drools	3
Constantly drools	4

Drooling Severity (DS) score	
☐ ≥ = 2:	

Drooling Frequency (DF) score	
☐ ≥ = 2:	

DSFS sum score (DS score + DF score)	
☐ ≥ = 6:	0

Have you been able to check all 4 boxes in step 1 and 2? Then XEOMEEN is reimbursed to treat this patient.

CHECKLIST STAGE 3: GICS SCORE

Step 3: GICS score (Global Impression of Change Scale score)

4 to 8 weeks after first XEOMEEN treatment, an improvement should be observerd for further reimbursement. Use the GICS score by answering the following question and checking the appropriate box: Compared to how the patient was doing just before the last injection into the salivary glands, what is the overall impression of how the patient is functioning now as a result of this treatment?

-3	-2	-1	0	+1	+2	+3
☐	☐	☐	☐	☐	☐	☐
very much worse	much worse	worse	unchanged	better	much better	very much better

Is the GICS score at least +1? Then XEOMEEN reimbursement is extended by 12 months at a maximum of 400 units for 4 treatments. Step 3 can be repeated for new 12 months extensions.

E-HEALTH PLATFORM

THANK YOU FOR YOUR ATTENTION

In case of any question:

FREDERIQUE.DEPIERREUX@CHULIEGE.BE / AUDE.LAGIER@CHULIEGE.BE

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REFERENCES

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