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Introduction and Objectives: The SIPEXI study investigated the efficacy and safety of repeated intraglandular incobotulinumtoxinA (incoBoNT/A) injections for sialorrhea associated with neurological disorders, also in young children aged 2-5 years (yrs).

Methods: SIPEXI was a prospective, multicenter, phase III study (NCT02270736) enrolling children with chronic sialorrhea associated with neurological disorders and/or intellectual disability. The younger cohort of 2- to 5-year-olds (N=35) was recruited after older children had been enrolled and assessed for safety. The 2- to 5-year-olds received up to 4 injection cycles (ICs) of incoBoNT/A with body weight–dependent doses according to weight classes of around 2 U/kg. The follow-up period was 16 weeks per IC. Efficacy outcomes included Carers’ Global Impression of Change Scale (GICS) mean ratings for 2- to 5-year-old patients (mean age 4 yrs; 57% with cerebral palsy; >94% with intellectual disability). Thirty-five patients were treated with incoBoNT/A, 33 out of 35 completed all 4 ICs. Good treatment effects were seen, although results were descriptive only (small sample size) (Figure). GICS ratings showed consistent improvements at all visits, with ratings around +1.0. Other endpoints supported the results. A sustained effect of incoBoNT/A was seen after repeated ICs, with notable improvements over time. The AE rate varied between the ICs (1st: 14.3%; 2nd: 21.2%; 3rd: 15.2%; 4th: 33.3%). Few related AEs and serious AEs (non-related) and no AESIs occurred. Most AEs were respiratory infections. No unexpected safety concerns arose.

Conclusions: Treatment of chronic sialorrhea with body weight–dependent doses of incoBoNT/A showed clinically relevant improvements and few and minor side effects in children aged 2-5 years.

Funding: Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany

Keywords: Botulinum neurotoxin type A; Chronic sialorrhea; IncobotulinumtoxinA; Pediatric

SAFETY RECOMMENDATIONS FOR TREATMENT WITH BOTULINUM TOXIN DURING THE COVID-19 PANDEMIC PREPARED BY THE ITALIAN BOTULINUM TOXIN NETWORK IN COLLABORATION WITH THE ACCADEMIA LIMPE-DISMOV, SISC, AND ANIRCEF ASSOCIATIONS

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Overview: In order to minimize the risk of virus transmission in the era of COVID-19, the Italian Botulinum Toxin Network, in collaboration with Accademia LIMPE-DisMov, ANIRCEF, and SISC, propose recommendations for good practice in performing botulinum toxin injections.

Recommendations to prevent SARS-CoV-2 infection:

Structural recommendations:

- Daily sanitization of areas to be used for botulinum toxin injections
- Take the patient’s body temperature at the entrance to the facility.
- Maintain appropriate social distancing in the waiting room.
- Provide healthcare personnel with personal protective equipment (PPE), such as surgical or FFP2 masks, footwear, headgear, disposable gowns, gloves and visors/glasses, and sanitizing agents.
- Provide patients with disposable materials, hand disinfectant, and surgical masks.

Patients should be instructed as follows:

- Come to the outpatient clinic with a protective surgical mask and nitrile gloves. (this also applies to persons accompanying patients)
- The person accompanying the patient must wear the protective surgical mask and, after delivering the patient, must wait outside the clinic or hospital during botulinum toxin treatment.

Related to the Procedure:

- The patient must disinfect the hands with hydroalcoholic or chlorine gel before entering the clinic. It is mandatory for the patient to wear non-sterile gloves and a surgical mask.
- Doctor and staff must remove all jewelry and personal items. Wash hands for at least 20 seconds with soap and water or alcohol solution. Put on the first pair of gloves. Put on footwear and headgear, then the disposable gown over the uniform, then a FFP2 mask; put on goggles or visor and the second pair of gloves.
- When finished with a patient and moving on to the next, follow the sequence indicated. Remove the second pair of goggles together with the disposable gown; remove the goggles or visor and sanitize them. Practice hand hygiene using soap and water or alcohol solution. In addition, if the botulinum toxin injection procedure involves the cranio cervical area or near the oral cavity, it is mandatory that
healthcare professionals change the FFP2 mask after each injection session, unless a protective visor is used.

- When finished with a patient and moving on to the next, clean all surfaces with which the patient has come into contact (eg, bed, chair) with hydroalcoholic disinfectants (70% ethyl alcohol) or chlorine-based disinfectants (0.1% sodium hypochlorite solutions). The most frequently handled surfaces should be protected with disposable barriers, which should be disposed of in special waste containers at the end of the session.
- Frequently exchange the air in the clinic between patients.

**Conclusions**: These recommendations indicate the minimum procedures necessary for safe botulinum toxin treatment in individuals who do not suffer from symptoms related to SARS-CoV-2 infection. New knowledge about SARS-CoV-2 infection may lead to changes in the recommendations for good practice.

**Keywords**: Botulinum toxin; COVID-19 pandemic; Italian Botulinum Toxin Network; Rete Italiana Tossina Botulinica; Safety Recommendations; SARS-CoV-2 infection

**References**
1. Ortega R, Gonzalez M, Nozari A, Canelli R. Personal protective equipment and Covid-19. N Engl J Med. 2020; 382(26):e105.
2. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): using personal protective equipment (PPE) (https://www.cdc.gov/coronavirus/2019-ncov/hcp/using-ppe.html).
3. van Doremalen N, Morris DH, Holbrook MG, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. N Engl J Med. 2020; 382: 1564-1567.

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**SPASTICITY TREATMENT WITH BOTULINUM TOXIN DURING THE COVID-19 PANDEMIC**

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**Introduction and Objectives**: Intramuscular botulinum toxin type A (BoNT-A) is an effective treatment for focal spasticity. Since the coronavirus disease 2019 (COVID-19) outbreak, all deferrable clinical activities have been suspended or postponed for several months worldwide. This monocentric, observational, cross-sectional study aims to investigate the impact of the COVID-19 pandemic on treatment of spasticity with BoNT-A in adult patients.

**Methods**: This study examined the BoNT-A spasticity treatments scheduled at a central hospital in the first six months of the COVID-19 outbreak in Portugal. We analyzed how many appointments were suspended and the extent of the delay of those that were rescheduled. Also, we compared the number of treatments that took place in that period with the number during the previous year.

**Results**: In the first three months of the COVID-19 outbreak, all scheduled treatments were either suspended or rescheduled. After that, there was a progressive return of the treatments, starting with the rescheduled ones (n=23) that took place with 2 to 6 months of delay. There were also some patients who missed their appointments (n=7) or that were discharged due to clinical reasons (n=12). By the end of the first semester, the total number of treatments, although with no immediate side effects noted, was about 50% less than the previous year.

**Conclusions**: The reorganization of non-urgent clinical activities that occurred due to the COVID-19 pandemic led to the interruption or delay of spasticity treatments. In the present study, the first three months had more repercussions, with a complete suspension of treatments, that were partially recovered in the second trimester. All the treatments that took place in the first semester had no immediate complications recorded, which is a good preliminary indicator of the safety of BoNT-A treatment during the COVID-19 outbreak, but further studies are needed.

**Keywords**: Botulinum toxin; COVID-19; Pandemic; Spasticity

**PREGNANCY OUTCOMES FOLLOWING EXPOSURE TO ONABOTULINTOXINA UPDATE: 29 YEARS OF SAFETY OBSERVATION**

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**Introduction and Objectives**: The safety of onabotulinumtoxinA during pregnancy remains an important topic for healthcare providers and their patients. This analysis evaluated pregnancy outcomes following onabotulinumtoxinA exposure to provide a cumulative 29-year update.

**Methods**: The Allergan Global Safety Database contains reports of onabotulinumtoxinA administration before/during pregnancy, including prospective (reported before outcome known) and retrospective (outcome known when reported) cases. The database was searched (1/1/90-12/31/18) for eligible cases where treatment occurred during pregnancy or ≤3 months prior to conception. To minimize reporting bias, prevalence rates for overall and major birth defects were estimated from prospective cases of live births only.

**Results**: Of 913 pregnancies, 397 (43.5%) were eligible with known outcomes. Maternal age was known in 215 cases, with 45.6% of mothers ≥35 years. Indication was known in 340 cases, with the most frequent being cosmetic (35.3%), migraine/headache (30.3%), and movement disorders (12.1%). OnabotulinumtoxinA dose information was known in 242 cases: 32.2% ≤50 U, 11.2% 50 U to <100 U, 40.1% 100 U to <200 U, and 16.5% ≥200 U. Of 105 prospective pregnancy cases with 197 fetuses, there were 152 (77.2%) live births and 45 (22.8%) fetal losses (32 spontaneous abortions, 13 elective abortions). Of the 152 live births, 148 (97.4%) had normal outcomes and 4 had abnormal outcomes. Among the 4 abnormal outcomes, there were 1 major birth defect, 2 minor fetal defects, and 1 birth complication. The prevalence rate for overall fetal defects was 2.6% (4/152, 95% CI: 1.0-6.6%) and 0.7% (1/152, 95% CI: 0.1-3.6%) for major fetal defects (3%-6% in the general population).

**Conclusions**: This 29-year retrospective analysis of safety data in onabotulinumtoxinA-exposed mothers demonstrated that the prevalence rate of