Protocol

**Title:** The Effect of Needle Size on Pain Perception in Patients Treated with Botulinum Toxin A Injections

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Table of contents

Table of contents
List of abbreviations

STUDY TITLE

1. STUDY DESIGN
2. STUDY POPULATION
   2.1 Inclusion criteria
   2.2 Exclusion criteria
   2.3 Subject Recruitment
3. STUDY PROCEDURES:
   3.1 Screening and treatment visit
   3.2 Visit Scheme
4. OUTCOME MEASURES
   4.1 Primary outcome measure
   4.2 Secondary outcome measures
5. STATISTICAL CONSIDERATIONS
6. REFERENCES
1. STUDY DESIGN

This prospective split-face, double-blinded, randomized control trial will compare the injection pain of Botulinum Toxin A (BTX-A) delivered for cosmetic use when a 30-gauge needle is used versus a 32-gauge needle. Female subjects, aged 25-70, with moderate dynamic forehead/glabellar rhytid complex will complete this study. Subjects will be screened, assessed, and randomized to be injected with onabotulinum toxin A using a 30-gauge needle on one side of the face and injected using a 32-gauge needle on the other side during their first clinic visit. All needles would be luer lock, ½ inch length, and attached to separate 1cc syringes. Injection depth would be 1-2mm, dermal, and the angle of incidence would be perpendicular. The order of the needle size used first will be randomized as well. Both the injector and the subject will be blinded to the needle size. An additional set of injections will be performed on the upper inner arm, with each arm randomized to each size needle. Subjects will fill out a pain score and characterize the discomfort from a list of 20 modifiers after each side is injected.

2. STUDY POPULATION

2.1 Inclusion Criteria
1. In good health
2. Is a female
3. Is 25-70 years of age
4. Has moderate dynamic forehead/glabellar wrinkles
5. Has willingness and the ability to understand and provide informed consent and communicate with the study staff

2.2 Exclusion Criteria
1. Younger than 25 or older than 70 years of age
2. Pregnant or lactating
3. Is a male
4. Has received the following treatments in the forehead or glabellar region:
   a. Botulinum toxin injections in the past 6 months
   b. Ablative laser procedure in the past 6 months
   c. Radiofrequency device treatment in the past 6 months
   d. Ultrasound device treatment in the past 6 months
   e. Medium to deep chemical peel in the past 6 months
   f. Temporary soft tissue augmentation material in the area to be treated in the past year
   g. Semi-permanent soft tissue augmentation material in the area to be treated in the past 2 years
   h. Permanent soft tissue augmentation material in the area to be treated
5. Has an active infection in the forehead or glabellar region (excluding mild acne)
6. Is allergic to cow’s-milk protein
7. Is allergic to albumin
8. Taking aminoglycoside
9. Is currently using anticoagulation therapy
10. Has a history of bleeding disorders
11. Has a mental illness
12. Unable to understand the protocol or to give informed consent
2.3 Subject Recruitment
The study staff will select subjects presenting to the Department of Dermatology at Northwestern University who meet the inclusion criteria.

3. STUDY PROCEDURES

3.1 Screening and Treatment Visit
- Female subjects who meet the inclusion/exclusion criteria will be selected to enroll in the study and consented.
- The subjects’ medical history will be recorded.
- Treatment randomization: The subjects’ left and right side (face and arms) will be randomized into either Treatment 1 (30-gauge needle) or Treatment 2 (32-gauge needle).
- Needle hubs will be blinded.
- Order of the needle size injected first will be randomized.
- The areas to be treated will be cleansed with alcohol.
- 100 unit vial of onabotulinum toxin A freshly reconstituted with room temperature 2.5cc benzyl alcohol containing saline will be injected into the bilateral forehead and glabella with no more than 24-40 units total per patient and total of 3-4 injections with the appropriate needle per side.
- The arms will be injected with saline only.
- The subjects will fill out a pain survey after each side has been injected.
- Subjects will fill out a survey to characterize discomfort after each side has been injected.
- The central glabella injection will be delivered last, after the pain survey.
- Ice packs will be applied per standard of care to decrease swelling and discomfort.

3.2 Visit Scheme

<table>
<thead>
<tr>
<th>Visit1 (screening, 1st treatment day, week 0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment for randomized area of both sides</td>
</tr>
<tr>
<td>Post treatment pain score</td>
</tr>
<tr>
<td>Subject characterize pain survey</td>
</tr>
</tbody>
</table>

4. OUTCOME MEASURES

4.1 Primary Outcome Measures
- Subjects will fill out a visual analog score (VAS) pain rating after each side is injected, but before the central glabella injection.
- Subjects will fill out the Short-form McGill Pain Questionnaire (SF-MPQ-2).

4.2 Secondary Outcome Measures
- Any adverse events will be noted and recorded.
5. STATISTICAL CONSIDERATIONS

At least twenty subjects will be screened and consented. Measurements obtained by both, VAS and SF-MPQ-2 will be compared. There is higher probability to potentially find significant variation in values for differences in SF-MPQ-2 values. Because this is a pilot study, values of 15 total summary points can be considered significant, and reason for additional examination.
6. REFERENCES


