Introduction

• Chemodenerivation of salivary glands with botulinum toxin A injection is a valuable tool in the treatment of pediatric sialorrhea.
• OnabotulinumtoxinA (Botox, Allergen) is the most common toxin used.
• Intral glandular injection is known to be effective and safe in pediatric patients.
• There is no consensus on a protocol for the optimal sites of injection and appropriate dosing.
• Objective: This systematic review aims to determine
  1) the optimal dosing and injection site of neurotoxin treatment for sialorrhea in the pediatric population and
  2) provide a protocol for this treatment.

Materials and Methods

• This review was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Protocol.
• PubMed, The Cochrane Systematic Reviews, Cochrane Center Register of Controlled Trials (CENTRAL), and EMBASE databases were queried to identify articles that evaluated the use of botulinum toxin type A for the treatment of sialorrhea in the pediatric population.
• A total of 405 studies were identified. After applying inclusion and exclusion criteria, 31 articles were included for full-text review.
• The Oxford Center for Evidence Based Medicine was used to determine the level of evidence of each study within our systematic review.

Results

• 1,287 total patients
• The most reported adverse reaction was dysphagia which was resolved in nearly all cases.
• Drooling Quotient and the salivary flow rate were the most frequently used objective measures. Drooling Frequency and Severity Scale and Visual Analog Scale were the most frequently used subjective measures.
• Three studies aimed to directly examine two-gland versus four-gland injections with two of the studies concluding four-gland injection was superior.
• There was significant heterogeneity in the characteristics of the intervention (site of injection, dose) and methods used to measure drooling outcomes.

Table 1. Summary of two- vs. four-gland injection studies

<table>
<thead>
<tr>
<th></th>
<th>Two-gland injections</th>
<th>Four-gland injections</th>
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</thead>
<tbody>
<tr>
<td>Number of studies</td>
<td>14</td>
<td>17</td>
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<tr>
<td>Level of Evidence</td>
<td>11 level 3, two level 4 and one level 5 study</td>
<td>Five level 2, 11 level 3 and one level 4 study</td>
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<td>Total # participants</td>
<td>899</td>
<td>388</td>
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<td>Dosing</td>
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<td>- 602 received a total of 50 units into their submandibular glands.</td>
<td>The most prevalent dosage was 60-100 units in 230 participants.</td>
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<td>- 262 received 30-50 units</td>
<td>The second most prevalent dosage was 100 units in 77 participants.</td>
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<tr>
<td>Outcome measures</td>
<td>Subjective</td>
<td></td>
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<tr>
<td>- Drooling Impact Scale (DIS), Drooling Frequency and Severity Scale (DFSS), patient and caregiver visual analog scale (VAS), and Teacher Drooling Scale (TDS)</td>
<td>Bottox injection with 100 total units over four glands resulted in a statistically significant reduction in DIS, number of bib changes per day, FFSS, and VAS at one-month follow-up.</td>
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<tr>
<td></td>
<td>Objective</td>
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<td>- salivary weight in grams over a specified period of time, drooling quotient, salivary flow rate, and the number of bib changes per day.</td>
<td>Bottox injection with 100 total units over four glands resulted in a statistically significant reduction in DIS, number of bib changes per day, DFSS, and VAS at one-month follow-up.</td>
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<tr>
<td>Results</td>
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<td>- Bottox injection with 30-50 total units resulted in a significant reduction in salivary flow rate, DIS, DFSS, and VAS compared to baseline at one-month follow-up.</td>
<td>Studies reported significant improvement in quality of life, improvement in speech and swallow function, and decreased hospitalization for respiratory distress.</td>
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<td>- Dosages below 30 units required booster injections one month after first injection</td>
<td>Bottox injection with 100 total units over four glands resulted in a statistically significant reduction in DIS, number of bib changes per day, DFSS, and VAS at one-month follow-up.</td>
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Adverse effects (AEs)

• The most significant AEs reported include severe dysphagia requiring hospitalization and aspiration pneumonia.
• Other AEs: xerostomia, mild-to-moderate dysphagia, dysthaesthesia and speech difficulties, coughing, chewing and feeding difficulties, salivary thickening, and weakening of oral musculature.
• Studies using a total dosage of 100 units or greater were more likely to report AEs.

Conclusion

• Two-gland injections into the submandibular gland may be safe and effective at a total injection dose of 50 units.
• Currently, there is not enough evidence comparing four-gland injections to two-gland injections; however, dosages totaling 60-100 units have been proposed as effective and safe.
• An optimal dosing protocol cannot be ascertained due to significant heterogeneity of interventions and outcome measures.
• Further research into two-gland vs. four-gland injections, and other neurotoxins are warranted in the pediatric population.

References