SEVERITY OF CEREBRAL PALSY AND INCIDENCE OF ADVERSE EVENTS FOLLOWING BOTULINUM TOXIN A INJECTIONS

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Introduction

Botulinum toxin A (BoNT-A) is a well-established treatment for hypertonia in children with cerebral palsy (CP). Adverse events (AE) reported following the use of BoNT-A are typically mild and self-limiting. The incidence of severe AE following BoNT-A has been estimated at 3.3-7.4%. In 2008 after concerns that systemic spread of the toxin may lead to respiratory distress and death, the FDA issued a black box warning. More research is needed to understand the risk factors for AE following BoNT-A. Severity of CP may be one such factor. This study aims to identify if severity of CP relates to incidence of AE after BoNT-A.

Methods

A review of data collected prospectively from a BoNT-A database and medical records of all patients attending the Kids Rehab BoNT-A clinic, an outpatient clinic at The Children’s Hospital at Westmead, was undertaken between July 2010 and June 2014. BoNT-A injections were performed under nitrous oxide sedation, and in a minority of cases with the addition of midazolam. Follow up with a clinician occurred a median of 26 days post injection (interquartile range: 21-35 days).

Data examined included AE at the time of the procedure and at follow up. Systemic AE were defined as lower respiratory tract illnesses, generalised weakness, dysphagia and death. Severity of CP was classified and grouped by the Gross Motor Function Classification System (GMFCS). The relationship between GMFCS group (GMFCS I, II & III vs GMFCS IV & V) and AE was analyzed using Generalized Estimating Equations.

Conclusions

18 children were hospitalised in the month following BoNT-A as a result of their systemic AE, 3 with life-threatening illnesses:

- 1 child (8.8 years, GMFCS V) had an adenovirus positive lower respiratory tract infection 14 days post
- 1 child (10.3 years, GMFCS IV) had an unexplained episode of decreased level of consciousness 30 days following BoNT-A in the context of previous episodes without preceding toxin injection
- 1 child (11.8 years, GMFCS V) died at home 28 days post, the case was not referred to the coroner

Table 1: Demographic details of children studied

<table>
<thead>
<tr>
<th>Injected Children</th>
<th>Children Attending Follow Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>591</td>
</tr>
<tr>
<td>Male</td>
<td>328 (55.5%)</td>
</tr>
<tr>
<td>GMFCS I, II &amp; III</td>
<td>353 (59.7%)</td>
</tr>
<tr>
<td>GMFCS IV &amp; V</td>
<td>238 (40.3%)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>178 (30.1%)</td>
</tr>
<tr>
<td>Gastrostomy</td>
<td>102 (17.3%)</td>
</tr>
<tr>
<td>History of aspiration pneumonia</td>
<td>54 (9.1%)</td>
</tr>
</tbody>
</table>

Results

During the study timeframe, 591 children had a total of 2219 BoNT-A injection episodes (Figure 1, Table 1). The mean BoNT-A (Botox®) dose was 9.6 U/kg (SD 4.8).

Figure 1: Flow chart of children studied

Procedural AE

- reported by clinicians in 130 (5.9%) episodes
- most commonly distress (1.8%), pain (1.7%), and nausea and/or vomiting (1.7%)
- no relationship between the rate of procedural AE and GMFCS level (p=0.38)

Follow up AE

- reported in 492 (22.7%) episodes
- most common AE were bruising (4.5%), upper respiratory tract infections (4.4%), local weakness (3.7%), pain (3.0%) and flu-like illnesses (2.9%)
- injection episodes involving children GMFCS I, II & III were significantly more likely to be associated with reports of local weakness (OR 0.19) and pain (OR 0.27)

Systemic AE

- occurred in 77 (3.6%) episodes
- increased likelihood of systemic AE in injection episodes involving children GMFCS IV & V (57 AE, 6.4%) compared with children GMFCS I, II & III (20 AE, 1.6%) (OR 4.30 (95% CI 2.42-7.62) p<0.0001) (Figure 2)

References


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