Botulinum toxin treatment for early onset esotropia

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Introduction

1) What is early-onset esotropia?
2) What is the point of botox?
3) What are our outcomes in Cape Town, South Africa?
Poll Q1: What is your level of interest in strabismus?

- Ophthalmic nurse
- Trainee ophthalmologist
- General ophthalmologist
- Paediatric ophthalmologist
Strabismus types  n=2566

- Esotropia: 68 cases
- Exotropia: 24 cases
- Paralytic: 4 cases
- Syndromes: 4 cases
Esotropias
Esotropias

- Congenital: 52
- Fully accom: 21
- Partial accom: 8
- Acquired: 10
- Sensory: 4
- CNS defects: 5

Total: 100
Congenital/ Infantile/ Early onset

- Present within 6 months of age
- Large angle, usually alternating ET
- No significant refractive error → non-accommodative
- No ocular pathology
- No brain pathology
- Associated features
Poll Q2: On average, how many children do you see with early-onset esotropia in your clinic per month?

• 0
• <5
• 5-10
• >10
Accommodative

- Fully or partially
### Esotropias – Big 5

<table>
<thead>
<tr>
<th>Sensory</th>
<th>n=70</th>
<th>CNS abnormalities</th>
<th>n=84</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cataract</td>
<td>11</td>
<td>Cerebral palsy</td>
<td>35</td>
</tr>
<tr>
<td>Optic atrophy</td>
<td>11</td>
<td>Developm delay</td>
<td>10</td>
</tr>
<tr>
<td>Toxoplasma</td>
<td>8</td>
<td>Meningitis</td>
<td>6</td>
</tr>
<tr>
<td>Coloboma</td>
<td>5</td>
<td>Hydrocephalus</td>
<td>3</td>
</tr>
<tr>
<td>Aniso amblyopia</td>
<td>5</td>
<td>Down syndrome</td>
<td>3</td>
</tr>
</tbody>
</table>
Poll Q3: What is the main racial profile of your patients with esotropia?

- Asian
- Black
- Mixed race
- White
Esotropias  n=1739
Squints in black children

• Disproportionately small numbers of black children with isolated strabismus (19%)
• Cannot be explained on the basis of referral bias, as equal access to healthcare
• Risk of isolated strabismus shown to be reduced in children of black maternal ethnicity

Squints in black children

• Nature and causes of this protective effect unknown

• Partly attributed to lower associated risk of hypermetropia

When black children do squint...

- 85% black South African children had esotropias
- Highest proportion reported to date
Esotropia: exotropia ratios

- **SA Black** (n=449): 85% Exotropia, 15% Esotropia
- **Egypt Arab** (n=957): 83% Exotropia, 17% Esotropia
- **SA Mixed** (n=1921): 71% Exotropia, 29% Esotropia
- **US White** (n=590): 65% Exotropia, 35% Esotropia
- **Cameroon Black** (n=137): 63% Exotropia, 37% Esotropia
- **Singapore Asian** (n=682): 72% Exotropia, 28% Esotropia
When black children do squint...

• Vast majority (74%) were congenital esotropes
• Vs 6% US white and 23% Singaporean Asians


Racial proportions: eso type

- Congenital: Black 74, Mixed 46, White 0, Asian 23
- Accommodation (Accomm): Black 9, Mixed 35, White 57, Asian 53
- Acquired: Black 5, Mixed 1111, White 17, Asian 4
- Sensory: Black 4, Mixed 4, White 7, Asian 3
- CNS: Black 8, Mixed 4, White 19, Asian 3
Poll Q4: At what age do you plan intervention for early-onset esotropia?

• < 1 year
• 1-2 years
• <5 years
• >5 years
Treatment options for early onset esotropia

• Early intervention
  • Toxin ASAP
  • Surgery ASAP

• Align by age 2 years

• Delayed intervention – operate before they get teased at school
3 steps to 3D

1. Bifoveal fixation - alignment of the eyes
2. Fusion - merging of the two slightly disparate images
3. Stereopsis - depth perception
Early intervention

- Better prognosis for achieving binocular function
- Concept of ‘locking on’
Taylor, Wright, Ing, Birch, Kushner

- Surgical correction of infantile esotropia >24 months is associated with poor stereopsis outcomes
Birch et al, J AAPOS, 2000

• Sensory outcome of congenital esotropic patients who had early surgery, some before 6 months, but also others at ages up to 24 months

• Those realigned <12 months of the onset of the esotropia had significantly better stereopsis

• Those with stereopsis were less likely develop consecutive exotropia than those without
Ing et al, J AAPOS, 2002

“Alignment within 1 year of age, or within 12 months of misalignment favourably affects the percentage of patients who develop stereopsis in the treatment of congenital esotropia”
Early intervention risks

**Toxin**
- Globe perforation
- Ptosis
- Induced vertical deviation
- Fixation preference and amblyopia

**Surgery**
- Globe perforation
- Need for 2 stage, or 3 or 4 muscle surgery
- Residual or consecutive deviation
- Fixation preference and amblyopia
What is Botox?

• Clostridium Botulinum
  Anaerobic spore forming G+ bacteria

• Produces potent neurotoxins
  7 serotypes (A to G)

• Inhibit pre-synaptic release of ACh

• Results in paralysis
  Onset: 2-3 days
  Maximal effect: 5 days
  Duration: 2-3 months
Poll Q5: When do you use botulinum toxin in your clinical practice?

- Blepharospasm
- Cosmetic reasons
- Ptosis
- Strabismus
- Never
Botox

• In ophthalmology, only type A and B are used
• Type A
  • Botox
    • Least diffusion, fewest side effects, use within 4hrs
  • Dysport
    • No fridge required
• Type B
  • Myobloc
    • Greater diffusion
    • Quicker onset
    • Shorter duration

• 1 unit Botox = 5 units Dysport = 100 units Myobloc
Uses of botox for Strabismus

• Diagnostic
• Therapeutic
  Paralytic
  Restrictive
  Childhood
First report: Botulinum treatment of childhood strabismus
Scott AB, Magoon EH, McNeer KW, Stager DR Ophthalmology 1990;97:1434-8

• 413 children, 2 months – 12 years old
• Outcomes >6mo follow-up
  61% aligned (<10PD) with an average of 1.7 injections
  Better results for ET (66%) than XT (45%)
  Better results for small (73%) rather than large (54%) angles
  Success rate not affected by prior injection
• Complications
  Ptosis 31%
  Induced vertical 16%
Botox in infantile esotropia

deAlba Campomanes AG, Binnebaum G, Campomanes EG. JAAPPOS 2010;14:111-6

• 442 children, <3 years of age
• Compared outcomes of
  322 children undergoing Botox (mean 1.5 y)
  120 children undergoing Surgery (mean 2.5 y)
• In botox group patients received
  1 injection: 49%
  2 injections: 41%
  3 injections: 10%
• Outcomes after 2 year follow-up
  45% aligned (<10PD) following botulinum toxin and 66%
  aligned following surgery
  <35PD pre-op: toxin=surgery
Advantages of botox over surgery

• Less invasive
• No scarring
• Can easily be repeated
• Cost-effective
Red Cross War Memorial Children’s Hospital Pilot Project

• 33 patients
• 1 year period from November 2014 to October 2015
• Assessing demographics, pathology, outcomes and complications
## Demographics

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Mean: 16 months; Range: 5 – 28 months (Outlier: 46 Months)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Male: 11 Female: 22</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td>Mixed race: 14 Black: 19 White: 0</td>
</tr>
</tbody>
</table>
# Pathology

<table>
<thead>
<tr>
<th>Refractive error</th>
<th>Mean: +2.7D (+0.5D - +5.5D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Given specs</td>
<td>7</td>
</tr>
<tr>
<td>PCT angle</td>
<td>Mean: 55PD ET (35 PD- 90PD)</td>
</tr>
<tr>
<td>IOOA</td>
<td>4</td>
</tr>
<tr>
<td>DVD</td>
<td>5</td>
</tr>
</tbody>
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Procedure in adults
Procedure in children

• Under GA with LMA
• 7 cases per monthly list
• 10 mins per case
• Grasp limbus with forceps
• Rotate globe temporally
Procedure in children

• Grasp MR insertion through conjunctiva

• Inject Botox -30 G needle
  EMG guidance not used

• Dosage
  5 units in 9 patients
  7.5 units in 22 patients

• Complications
  No complications intra-op
## 2 week side-effect assessment

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Exotropia (90%)</td>
<td>30</td>
</tr>
<tr>
<td>Ptosis (90%)</td>
<td>Unilateral in 10 patients, Bilateral in 21 patients</td>
</tr>
<tr>
<td>Vertical deviation (3%)</td>
<td>1</td>
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### 3 month assessment

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Patients in study</td>
<td>28</td>
</tr>
<tr>
<td>Manifest success &lt;10PD (50%)</td>
<td>15</td>
</tr>
<tr>
<td>PCT angle</td>
<td>Range: 40PD ET – 120 PD XT</td>
</tr>
</tbody>
</table>
| Fusion (18%)             | Present: 3  
                           | Not present: 14  
                           | Not noted: 11  |
## 1 year assessment

<p>| | |</p>
<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Patients in study</td>
<td>17</td>
</tr>
<tr>
<td>Manifest success (30%)</td>
<td>6</td>
</tr>
<tr>
<td>APCT angle</td>
<td>Mean: 20PD ET (c/w Pre-op mean: 55PD ET)</td>
</tr>
<tr>
<td>Fusion (12%)</td>
<td>2</td>
</tr>
<tr>
<td>Consecutive XT</td>
<td>0</td>
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</tbody>
</table>
## Further management

<table>
<thead>
<tr>
<th>Management</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectacles given</td>
<td>7</td>
</tr>
<tr>
<td>Repeat botox</td>
<td>4</td>
</tr>
<tr>
<td>Time till repeat</td>
<td>Mean: 9 months (4 – 15 months)</td>
</tr>
<tr>
<td>Surgery performed</td>
<td>3</td>
</tr>
<tr>
<td>Time till surgery</td>
<td>Mean: 14 months (10 – 17 months)</td>
</tr>
<tr>
<td>Total follow up</td>
<td>Mean: 8 months</td>
</tr>
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Summary

• Botox for early onset esotropia appears to be safe and effective
• Ptosis is common early post-op
• 30% success rate at 1 year
• Repeat botox may be indicated earlier
• Angle significantly reduced in most cases
• May reduce the number of muscles needing to be operated
Conclusions

• Early onset esotropia is common in our community
• There is a point to Botox
• Earlier intervention appears to increase the chance of a good sensory outcome, which increases the likelihood of longterm stability of alignment
• Preliminary results of its use at Red Cross War Memorial Children’s Hospital are encouraging
Thank you