



# Golden Indications and an Overview on the Use of Botulinum Toxin in Strabismus

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## Abstract

Botulinum toxin A (BTXA) is considered a pharmacological agent that may provide an alternative treatment to surgery in strabismus. It can be used as both a diagnostic and therapeutic agent in various concomitant, paralytic, and restrictive disorders. The major advantage of BTXA treatment is that it is non-invasive and does not impact the patient's chance for future surgery in case of an unfavorable response. In some selected disorders, BTXA has become the primary choice of treatment, whereas surgery is found to be more effective in others. Accumulated knowledge and experience have demonstrated that BTXA is more than merely an alternative treatment and has additional specific indications such as in unstable deviations and as an adjunct to surgery. Patients with recurrent deviations despite multiple surgeries are also good candidates for BTXA treatment. Although the major expectation is to obtain a permanent result, BTXA can also be used as a maintenance treatment. This paper mainly focuses on the current indications for the use of BTXA in strabismology, with special emphasis on ideal first-choice applications referred to as "golden indications," within the scope of the author's own experience with the use of BTXA over 30 years.

**Keywords:** Botulinum toxin, strabismus, strabismus surgery, paralytic strabismus, pharmacological treatment of strabismus

## Introduction

Botulinum toxin A (BTXA) has been used for the pharmacological treatment of strabismus for over three decades. In most of the strabismus literature it is mainly regarded as an alternative to surgery depending on the choice of the strabismologist. However, accumulated knowledge and experience have demonstrated that BTXA is not only an alternative therapy but has some additional indications where surgery is not a good option.<sup>1,2</sup> Despite a dearth of randomized controlled trials, BTXA seems to have comparable results with surgery in selected motility problems.<sup>3,4,5</sup> In this paper, the best indications for the use of BTXA, hereafter referred to as "golden indications," will be highlighted with literature results and the author's own experience with the use of BTXA in strabismus over 30 years.

## Historical Perspective

The first person to conceive of injecting a pharmacological agent into the extraocular muscles (EOM) to weaken their function was Conrad Behrens, who had unsuccessful results with alcohol due to tissue necrosis and permanent paralysis.<sup>6</sup> Scott<sup>6,7</sup> found that BTXA could be used for the treatment of strabismus after testing various drugs in the EOM of monkeys. Human studies were started in 1977, and US Food and Drug Administration approval was obtained in 1989 for its use in adults and children over 12 years of age with strabismus.

## Mechanisms of Effect

Eight antigenic types of botulinum toxin have been identified and type A is used in strabismus. BTXA blocks acetylcholine release, interferes with calcium metabolism, and creates a "chemodenervation" effect. After injection into an EOM, the maximum effect is reached in 5-7 days and the paralytic effect lasts for 2 months. The overall weakening effect of BTXA lasts for 6-9 months. During the effect of BTXA, a relative contracture of the antagonist is expected to occur.<sup>8</sup>

*In memory of John P. Lee and Alan B. Scott...*

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Although there are a number of new products either on the market or on the way, the main commercial BTXA products in the market with nearly worldwide approval are Botox (onabotulinumtoxin A, Allergan), Dysport (abobotulinumtoxin A, Ipsen), and Xeomin (incobotulinumtoxin A, Merz).

BTXA has a temporary effect on EOM but may result in a permanent decrease in deviation. Possible mechanisms of this permanent effect may be related to alterations in sarcomer number during the effect of BTXA, immunohistochemical changes, central adaptive mechanisms that manifest with improved binocularity, and as we suggested, a “traction suture-like” effect during the overcorrection period.<sup>9,10,11,12</sup>

### Injection Techniques and Dosage

The gold standard method of BTXA injection is under topical anesthesia with electromyographic (EMG) guidance using a monopolar needle electrode to ensure the injection is administered to the target tissue, and it is mainly an outpatient treatment. The injection can also be performed using an insulin syringe by grasping the EOM with Mendonça forceps, although this inevitably means a more anterior injection and more discomfort for the patient. This method works well in medial rectus (MR) muscles without previous recession. In EOM with previous recession, grasping the EOM is challenging and there is less chance of reaching the target tissue. Inferior rectus (IR) muscle injections should better be performed with EMG guidance through the lower eyelid while the EMG signal is heard on depression. Without EMG guidance, it is not possible to determine whether the injection is made in the inferior oblique or IR muscle. Sub-Tenon injections are imprecise and have a higher risk of spread to neighboring EOM. Injection under direct visualization through a surgical opening is an invasive method which is antithetical to the non-invasive nature of BTXA treatment and should only be considered if the injection is done in combination with surgery.

In children, the injection should be done under ketamine anesthesia in order not to alter the EMG signals. We prefer injection without EMG control only in infants.

The usual dose for EOM is 2.5-10 units (U) and unlike the skeletal muscles, the same dosage may be used for both Botox and Dysport in the EOM. There is no real dose-response curve for BTXA injection. Our preferred standard dose is 5 U; we reduce the dose to 2.5 U in infants and increase the dose up to 10 U in thyroid orbitopathy. Larger doses result in more spread to adjacent tissues and increased complications rather than increased effect, and early overcorrection is a good indicator for a better outcome.<sup>13,14</sup> If the desired effect is not achieved, a repeat BTXA injection can be added in the 1-week follow-up visit.

The most commonly injected EOM are the MR, lateral rectus (LR), and IR. In general, oblique muscle injections are not as successful as rectus muscles.

### Advantages of BTXA Treatment

The major advantages of BTXA treatment over surgery are the non-invasive nature of the treatment, absence of scar tissue

formation, and ability to perform unlimited repeat injections without interfering with future chance of surgical treatment. BTXA injection may be used as a maintenance treatment in patients with multiple failed previous surgeries and those who refuse surgery for any reason. It is an outpatient treatment in adults and requires a very short period of ketamine anesthesia in children. In busy clinics, the cost of the drug does not incur much financial burden.

### General Indication Categories

Although the temporary effect of BTXA is regarded as a disadvantage, it is advantageous in certain cases where surgery is not an option, such as unstable deviations and those with the risk of postoperative diplopia. The use of BTXA during the acute phase of paralytic, restrictive, or concomitant deviations is an additional indication, as surgery is not an alternative during this unstable period.

The major indications of BTXA may be categorized as diagnostic use, therapeutic use, and adjunctive use to increase the success of surgery.

### Diagnostic Use of BTXA

Botulinum toxin may be used to assess the potential function of the paretic muscle, which may be masked by antagonist contracture. If the function of the paretic EOM increases with release of the contracture of the antagonist muscle by BTXA injection, this alters the surgical plan.<sup>15</sup>

Assessment of postoperative diplopia risk is another major indication for diagnostic use. Patients who report diplopia in the postoperative diplopia test may not have diplopia when their eyes are surgically aligned, but some of those patients have permanent diplopia after surgery. Injection of BTXA provides a temporary orthophoric period and enables the identification of those who will have a permanent diplopia problem.<sup>16,17</sup>

Central fusion disruption is a challenging problem with an unfavorable outcome.<sup>18,19,20</sup> Intractable diplopia related to central fusion disruption is a golden indication for BTXA.<sup>21,22,23</sup> The main advantage of BTXA compared to prisms is to provide an orthophoric period under real-life conditions. Even conventional prisms have a negative effect on quality of vision, albeit to a lesser extent than Fresnel prisms, and this effect increases with prism power.<sup>24,25</sup> We previously reported a group of patients with intractable diplopia and strabismus related to intracranial problems or long-term uncorrected aphakia who underwent BTXA injection into the appropriate EOM.<sup>23</sup> In our study group, 64% of the patients regained fusion, some of whom achieved a permanent cure after BTXA injection. Patients who do not have the capacity for fusion should be identified before considering any surgery, and BTXA is an excellent choice that serves this purpose.

### Therapeutic Use of BTXA

BTXA injection is used therapeutically in various types of concomitant, restrictive, and paralytic strabismus. The list of the indications for BTXA are summarized below, with special emphasis on golden indications.

### BTXA in concomitant deviations

BTXA can be used as a therapeutic agent in various types of concomitant strabismus. In concomitant strabismus, BTXA is more effective for moderate angles. In some motility problems, repeat injections are required as maintenance therapy, where in others one or two injections provide a permanent decrease in the deviation. Binocular fusion is the determinant mechanism that locks the correction of the eyes for a permanent effect. However, even in patients who require regular injections, there is a tendency toward longer intervals and reduced deviation.<sup>26,27</sup>

The results of BTXA therapy were found to be similar in children and adults.<sup>28,29,30,31</sup> Our results in childhood strabismus revealed that better outcomes are achieved in those with small angles and binocularity. Additionally, patients without binocularity who have small angles and high risk of consecutive deviations are also good candidates for BTXA therapy.

The indications for BTXA in concomitant deviations can be summarized as below:

- Infantile esotropia
- Deviations associated with neurological impairment/cerebral palsy
- Residual/consecutive deviations
- Multiple previous surgeries
- Intermittent deviations
- Convergence insufficiency
- Convergence spasm
- Small-angle deviations
- Sensory eso/exodeviations
- Acute comitant esotropia
- Cyclic deviations

In infantile esotropia, the results are comparable to surgery, with better outcome in deviations  $\leq 30$  prism diopter (PD) and early injections.<sup>32,33,34,35,36,37</sup> In larger angles, surgery was found to be more successful. Infantile esotropia with associated ocular abnormalities such as microphthalmos represents one of the golden indications of BTXA.

In childhood strabismus, another first-choice application for BTXA in concomitant deviations are cases associated with cerebral palsy or other neurological problems or developmental delay. In this group of patients there is a tendency to delay surgery because of the high risk of consecutive deviations and the potential risks of full general anesthesia in surgery. However, these patients may have significant gains in motor skills with the alignment of their eyes, and improved binocularity may yield permanent results. Previous reports suggested that these patients may benefit from BTXA injection.<sup>38,39,40</sup> In our recent series including 50 patients with neurological impairment, we found that the overall success rate was 60%, with better outcome in esodeviations and shorter duration of strabismus.<sup>40</sup> Our results demonstrated that instead of delayed surgery, these patients should receive prompt BTXA treatment for a better outcome. Therefore, such cases are considered a golden indication of BTXA in our clinical practice.

In patients who have undergone multiple previous surgeries but still have recurrent deviation, BTXA is a very good option to keep the eyes aligned and improve quality of life.<sup>26,27</sup> In this group who seem to have no other chance for surgery, BTXA is our first-line treatment as a golden indication, but repeat injections are usually required in these patients.

In intermittent exotropia, the results of BTXA injection are encouraging in children.<sup>41,42,43</sup> In adults, we prefer BTXA for those who had a recent decompensation of intermittent exotropia.

Sensory eso- or exodeviations represent another difficult group who may need to have multiple surgeries because of recurrent deviations related to poor visual acuity in one eye and lack of binocular fusion. These patients may present with very large deviations and in those cases our preference is to perform surgery first and then use BTXA in case of recurrence before the deviation increases.

Late-onset acute comitant esotropia has become a rising problem in recent years because of excessive screen use. BTXA provides an orthophoric period to allow the binocular system to recover and may provide a permanent cure. In comparative studies with surgery, similar success rates were observed in both adults and children.<sup>44,45,46,47</sup> One comparative study showed a lower success rate with BTXA, but this study included a wide range of age groups.<sup>48</sup> For late-onset acute comitant esotropia related to excessive screen use, the author's first-line treatment as a golden indication is BTXA injection, while surgery is reserved for those who do not achieve a permanent cure with BTXA.

Cyclic deviations represent a rare form of strabismus. Surgical treatment based upon the deviation on squinting days carries the risk for overcorrection. The results with BTXA injection were found to be encouraging in previous reports, including ours.<sup>49,50,51</sup> In our case study with long-term follow-up of 8 years, we found that BTXA may either provide a cure or break the cycle.<sup>51</sup> Thus, we consider cyclic deviations among the golden indications.

### BTXA in paralytic strabismus

The use of BTXA during the acute stage of paralytic deviations represents an additional indication of BTXA use where surgery is not an alternative. In order to consider any surgery, a period of at least 6 months is required and this period may increase to up to 1 year, especially in third nerve palsy because of the possibility of late spontaneous recovery. BTXA injection during the acute stage of paralytic deviations aims to provide symptomatic relief of diplopia, decrease the deviation and abnormal head posture, reduce the antagonist contracture in large angles, and assess the fusion potential in those with central fusion disruption.<sup>23,52,53,54,55</sup>

The most common golden indication for BTXA injection is sixth nerve palsy, in which it provides rapid relief of symptoms. BTXA was found to have no effect on spontaneous recovery.<sup>56,57</sup> However, in total sixth nerve palsy, those who had BTXA treatment during the acute phase were found to have smaller final deviation compared to conservatively followed patients, which represents an advantage for further surgery.<sup>58</sup>

In chronic cases, BTXA injection into the MR muscle in combination with vertical rectus transposition reduces the risk of anterior segment ischemia.<sup>59</sup> BTXA injection may be performed either before or after surgery. Injection before surgery is advantageous to assess potential LR function and perform transposition surgery under the full effect of BTXA. The disadvantage is the overcorrection period, which can sometimes last more than 6 months. The benefit of postoperative BTXA injection is the ability to see the transposition effect first and then decide whether to inject or not. Our preferred method in cases who present in the chronic stage with a large angle of deviation is to administer the BTXA injection one week before surgery, while in those with moderate angles we prefer to perform transposition first.

In a primary case of total sixth nerve palsy, our approach is to inject BTXA during the acute period. In those with deviations under 35 PD 6 months after BTXA injection, the author's preference is modified Nishida transposition without further MR weakening, adding BTXA later if required. In a multicentric study on modified Nishida transposition in sixth nerve palsy, we found that the mean correction with modified Nishida transposition alone was 29.4 PD and increased to 62.6 PD when combined with MR recession or MR BTXA and 95 PD when combined with MR recession augmented by BTXA.<sup>60</sup>

In total third nerve palsy, LR contracture and orbital fibrosis are the major challenges.<sup>52</sup> BTXA may help to prevent contractures and thus increase the likelihood of success in future surgical treatment. In chronic cases it may also be used to function as traction sutures in combination with large recess-resect and superior oblique transposition surgery.<sup>61</sup>

BTXA is not in common use for fourth nerve palsy. Injections to the ipsilateral inferior oblique, contralateral IR for undercorrections, and ipsilateral IR for overcorrections after SR recession may be considered.<sup>54,55,62,63,64,65</sup> We do not use oblique muscle injections. In patients with long-standing fourth nerve palsy and SR contracture, SR recession may cause overcorrection, and ipsilateral IR injection in the acute phase may provide a permanent cure.<sup>65</sup> In a small case series, we found that BTXA injection into the SR in combination with inferior oblique disinsertion may be effective in the long term in patients with a large angle of deviation and SR contracture to prevent overcorrection.<sup>66</sup>

BTXA is effective in supranuclear palsies either in the acute or chronic phase.<sup>67,68,69</sup> These patients may have associated problems that limit their chance for surgery and BTXA may be very helpful both for symptomatic relief and a possible cure.

#### **BTXA in restrictive strabismus**

Of the congenital restrictions, BTXA injection may be beneficial in Duane syndrome.<sup>70,71,72</sup> It is known that the innervational pattern does not change in Duane syndrome. However, the balance between co-contracting EOM and secondary contracture may show alterations that can result in increased abnormal head posture and primary position deviation. BTXA may help in permanently reorganizing the paradoxical contractile forces. BTXA seems more effective when used at young ages, preferably during infancy.<sup>70</sup> It may also be helpful

to control postoperative over- and undercorrections. In Duane syndrome, our indications for BTXA treatment are abnormal head posture during infancy and recently increased abnormal head posture at any age as well as residual and consecutive deviations.

In acquired restrictive problems, BTXA cannot release fibrotic changes but may be useful if fibrosis is not fully developed. Thyroid orbitopathy, orbital myositis, strabismus after retinal detachment surgery, postoperative restrictions, and the acute stage of adherence syndrome are indications for BTXA in selected cases.<sup>12,73,74,75,76</sup> Thyroid orbitopathy is a common restrictive problem and surgery must be performed during the inactive stage of the disease. However, the process of becoming fully inactive may be quite prolonged, and BTXA treatment may offer these patients symptom relief during this active inflammatory period before fibrotic changes develop.

#### **Specific Indications of BTXA as an Adjunct to Surgery**

BTXA may be used to increase the success of surgery in following categories:

1. In combination with recession to augment the effect of recession or recess-resect surgery,
2. Instead of recession to reduce the risk of anterior segment ischemia in transposition procedures,
3. As a replacement for traction sutures to overcome fibrosis or contracture problems,
4. To rescue surgical failures and complications.

#### **BTXA to augment the effect of recession**

BTXA may be used in combination with recession to augment the effect of recession or recess-resect surgery, which provides a greater effect without the disadvantage of permanently reduced EOM function in supramaximal recessions.<sup>77,78</sup> In our previous study we obtained satisfactory long-term results both in eso- and exodeviations with large angles with BTXA injection into the recessed muscle during surgery.<sup>77</sup> Lueder et al.<sup>79</sup> reported that BTXA-augmented bimedial recessions in infantile esotropia with large angles over 65 PD had a higher success rate with a lower rate of consecutive exodeviation in the long term compared to supramaximal recessions.<sup>80</sup> In another study of infantile esotropia with large angles, the authors calculated the numerical effect as 5.7 PD/mm and 4 PD/mm in BTXA-augmented and non-augmented recessions, respectively.<sup>81</sup>

We previously reported that in sensory eso- or exodeviations, BTXA effectively increased the effect of recession in recess-resect surgery in the long term.<sup>82</sup> The major advantage of combining BTXA with recession is to avoid the need for supramaximal surgeries or third and fourth rectus muscle surgeries in sensory deviations where surgery is not desired in the "good eye."

#### **BTXA instead of recession to reduce anterior segment ischemia risk**

In paralytic cases where full muscle transpositions are required in combination with third rectus muscle recession, BTXA can be used instead of recession. BTXA may also be used in some traumatic cases with EOM muscle and ciliary vessel damage to weaken the antagonist muscle with less risk of anterior segment ischemia.

### BTXA as a replacement for traction sutures

Traction sutures are used in the treatment of complex strabismus problems to overcome severe contracture and orbital fibrosis. It is preferred they remain in place for 6 weeks, which is an unpleasant period for the patient. Augmentation of recession either in combination with transposition or with a large antagonist resection provides significant overcorrection during a similar period of time that serves as traction sutures, an effect referred to as “pharmacological traction” (Figure 1). In our clinical experience we found this method very effective and well-tolerated in third nerve palsy, long-standing sixth nerve palsy, and traumatic cases.<sup>1,61</sup> Using BTXA in combination with resection or transposition to obtain a traction suture effect has become one of our golden indications.

### BTXA to rescue surgical complications

Over- and undercorrections are the most common problems after surgery, and BTXA may provide a “pharmacological adjustment” effect.<sup>83,84</sup> Both in acquired and infantile esotropia, BTXA was found to have an effect equal to surgery in the rescue of failures, and the BTXA group had better results when injections were given within the first 3 months postoperatively.<sup>85,86</sup> In postoperative injections, the mechanism of effect is mainly through alteration of mechanical contractile forces and soft tissue healing in the early phase and a central adaptive mechanism in the chronic phase.<sup>1,2,84</sup> In reoperations with stretched scars and or slipped muscles, the muscle becomes stiff and with advancement or resection of the stretched scar, overcorrections may occur despite adjustable sutures. BTXA is very useful to release the contracture in the early postoperative period and this is one of our golden indications.<sup>76</sup>

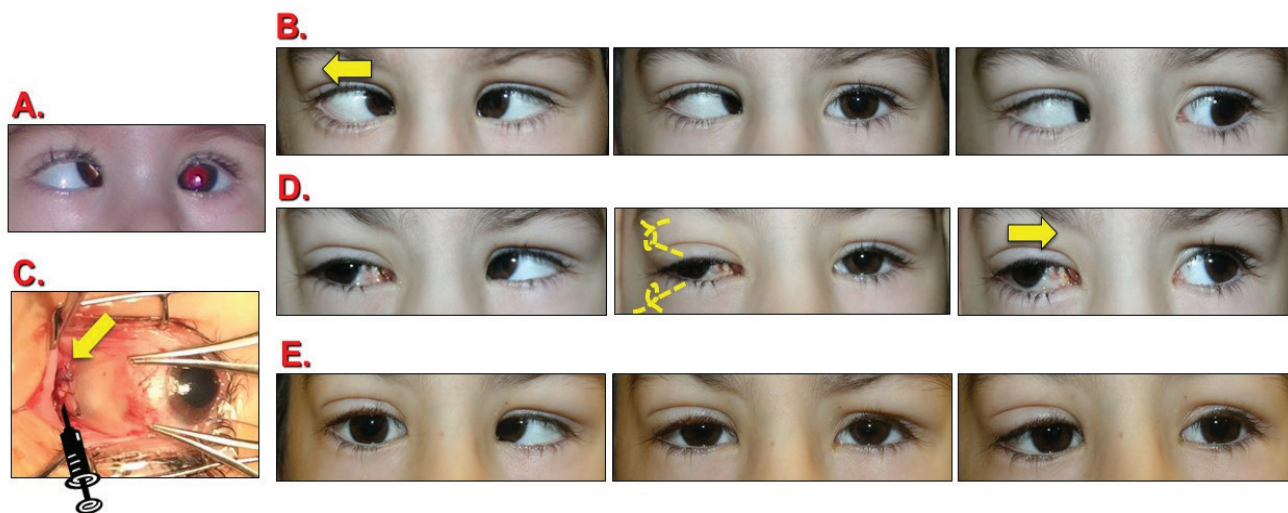
In cases with a lost muscle problem, it was shown that antagonist contracture develops in as little as 2 weeks if surgery

is delayed for any reason.<sup>87</sup> Relaxation of the antagonist by BTXA injection may be useful for a successful outcome with the additional benefit of allowing more anterior attachment of the soft tissues surrounding the lost muscle to the globe (Figure 2).<sup>76,88</sup> In late interventions where any transposition surgery is being considered after failed attempts to find the lost muscle, BTXA injection is the appropriate choice to release the antagonist contracture to avoid anterior segment ischemia. Lost muscle with delayed surgery is considered among our golden indications of BTXA.

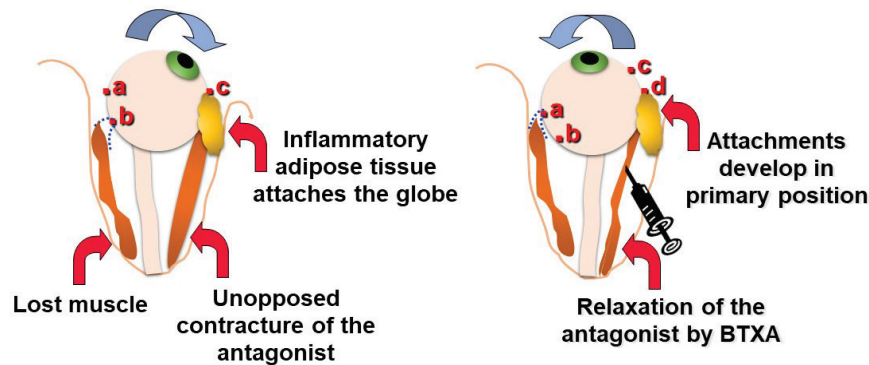
We have previously reported that BTXA may be highly effective in adherence syndrome, a very challenging complication, if injection is performed during the acute inflammatory period before the development of fibrosis.<sup>12,76</sup> If the eye can be kept in primary position during the inflammatory period, the attachments of fatty tissue develop more posteriorly, thus resulting in less limitation of ocular motility. Therefore, the acute period of adherence syndrome is among the golden indications of BTXA if used with appropriate timing (Figure 2).<sup>1</sup>

### BTXA in Posttraumatic Strabismus

In posttraumatic EOM damage and/or adherence syndrome, BTXA injection to the appropriate EOM may be very useful either to reduce the risk of anterior segment ischemia, prevent antagonist contracture, or reduce adherence syndrome-related motility problems.<sup>1,2</sup> In the acute stage, BTXA injection may keep the eye in primary position, thereby reducing contracture of the antagonist EOM and allowing soft tissue healing with the eye in primary position, which may reduce the effect of orbital fibrosis on ocular motility (Figure 2). In the chronic stage, it may be used as maintenance therapy or to reduce the anterior segment ischemia risk in multiple rectus muscle surgery.



**Figure 1.** (A) A child with history of preterm birth had sixth nerve palsy in the right eye related to intracranial hemorrhage at 5 months of age. (B) The child was not treated and returned at 7 years of age with a very large right esotropia and severe limitation of abduction. There was severe antagonist contracture and orbital fibrosis. (C) The medial rectus muscle was recessed 14 mm from the insertion and botulinum toxin A was injected in combination with modified Nishida transposition in the same session. Forced abduction test was still positive on abduction at the end of operation. (D) On postoperative day 13, there was severe overcorrection with limitation of adduction. The effect resembled that of traction sutures. (E) At postoperative 16 months, the result was stable with limited abduction and moderate limitation of adduction



**Figure 2.** The mechanism of effect in lost muscle and adherence syndrome. When an extraocular muscle is lost, contracture of the antagonist develops and pulls the globe. Botulinum toxin A injection into the antagonist extraocular muscle in the acute phase prevents antagonist contracture and keeps the eye in primary position. Thus, any possible attachments around the extraocular muscle attach to the globe more anteriorly (at point “a” instead of “b”). Similarly, in adherence syndrome the inflammatory adipose tissue reaction pulls the globe and limits ocular motility. Botulinum toxin A injection during the acute phase keeps the eye in primary position and allows the attachments to develop at a more posterior point (“d” instead of “c”), thereby reducing limitation of ocular motility

BTXA: Botulinum toxin A

### Complications of BTXA Treatment

The main problem with BTXA injection is related to its spread to neighboring tissues, with ptosis seen in 9%-42% of cases and neighboring EOM affected in 8.3%-18.5% of patients.<sup>89</sup> It was reported that ptosis occurs less when BTXA is injected with sodium hyaluronate.<sup>90</sup> Although diplopia in the acute phase due to overcorrection or limitation of ocular motility may be bothersome for some patients, this is actually not a complication but the natural effect of BTXA. Tonic pupil may occur in 0.16%-11% of patients and is likely related to needle injury rather than the effect of BTXA.<sup>91</sup> Accommodation deficiency, subconjunctival hemorrhage, and retrobulbar hemorrhage are other possible complications of BTXA treatment. The least common but most serious complication is scleral perforation, which was reported at a frequency of 0.28% in one series.<sup>89</sup> We have not observed scleral perforation in our clinical practice. Patients with excessive scar tissue and those with myopia-related large globes are at high risk for globe perforation. In an experimental study it was demonstrated that BTXA was non-toxic for the retinal tissue.<sup>92</sup>

### Problems with BTXA treatment

Despite the many advantages of BTXA treatment there are some problems that limit its use in some instances. These problems can be summarized as follows:

- Difficulty reaching the target tissue: Despite EMG guidance this is still a problem.
- Uncertainty of the effect during the early post-BTXA period: Full paralytic effect is obtained in some cases, whereas only a decrease of the deviation without overcorrection or limitation of ocular movement may be obtained in others.
- Inefficiency in established fibrosis: The decision to perform BTXA injection must be made quickly in

most cases to obtain a benefit before fibrosis has fully developed.

- Possibility of repeat injections: If the desired effect is not obtained, repeat injections are required during the early post-injection period, which may be a significant problem in children especially. In adults, an additional dose at the 1-week post-injection visit usually solves the problem in those with inadequate effect.
- Off-label use in children.
- Cost/insurance problems-varies by region.
- Lack of dose-response grading: In the author's view, the effect is more related to reaching the target tissue than the applied dose.

### Golden indications for BTXA treatment in strabismus

Considering all the advantages and disadvantages of BTXA treatment and the author's experience using this agent in clinical practice, the golden indications of BTXA can be summarized as follows:

- Late-onset acute comitant esotropia,
- Unstable concomitant deviations with cerebral palsy,
- Infantile esotropia with associated abnormalities,
- Paralytic/restrictive strabismus-acute phase,
- Early over- and undercorrections,
- Early adherence syndrome,
- Lost muscle with late intervention,
- Intractable diplopia related to central fusion disruption,
- The need to weaken a rectus muscle in the presence of the risk of anterior segment ischemia,
- Recurrent deviations despite multiple previous surgeries,
- Cyclic deviations.

## Conclusion

In summary, there are five indication categories of BTXA treatment in strabismus:

- Alternative to surgery and prisms in selected concomitant, restrictive, and paralytic deviations,
- A necessary additional agent in acute deviations where surgery is not an alternative,
- Good choice in surgical failures,
- Good choice to increase surgical success,
- Only choice if surgery is not an option for any reason.

In conclusion, BTXA treatment has become the primary option in certain strabismus problems. Strabismologists are recommended to be familiar with BTXA treatment, as it has gained its own non-surgical indications and has an adjunctive role in the management of challenging motility problems rather than being only an alternative treatment based on physician preference.

### Ethics

**Peer-review:** Internally peer-reviewed.

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