



Benefit of botulinum toxin in the management of strabismus

Written with the assistance of Arnaud SAUER, Pierre LEBRANCHU, Sophie ARSENE et Claude SPEEG and validated by the French Association of Strabologie and Pediatric Ophthalmology (AFSOP)

Botulinum toxin A is used in ophthalmology since the 1970s. Its indications in strabismus are still limited and often discussed (Rowe JF, Noonan CP. Cochrane Databas Syst Rev 2012). Botulinum toxin A may be indicated in oculomotor palsy and early strabismus. Only physicians trained in the use of botulinum toxin can currently propose its use.

I. Botulinum toxin A and oculomotor palsy

Benefits

Botulinum toxin A could have the advantage of rapidly restoring fusion in patients with oculomotor palsy and thus limiting diplopia duration. It has been approved for the treatment of oculomotor disorders after the age of 12 years.

Indications

Its indications are primarily intended for recent palsy (less than 6 months). Its use in patients with chronic palsy is anecdotal and discussed (only when muscle spasm is present).

- In patients with **sixth nerve palsy**, botulinum toxin A is injected into the ipsilateral medial rectus muscle . This treatment may be discussed when the palsy persists beyond 3 months. However, studies have shown limited benefits with a similar efficacy at 6 months and 1 year compared to the conservative treatment (prisms and / or occlusion). It is not established whether injecting botulinum toxin improves the rate of recovery, but it probably enables faster recovery in some patients (Kao et Chao, J Ped Ophthalmol Strabismus 2003; Holmes, JAAPOS 2003).
- Regarding **third or fourth nerve palsy**, the results are anecdotal. The use of botulinum toxin is limited to particular cases and to subspecialisation in this indication (Crouch, Cur Opin Ophthalmol 2006).

Conclusion

Botulinum toxin A may be proposed in some cases of sixth nerve palsy to enable faster recovery.

II. Botulinum toxin A and early strabismus

Definition

Early strabismus is a strabismus occurring during the maturation phase of binocular vision (in practice before the age of 6-9 months). Its frequency is around 1%.

Signs

Early strabismus syndrome includes sensory and oculomotor signs.

The pathognomonic sensory sign is the irreversible absence of normal retinal correspondence. Amblyopia is present in 10-50% of cases.

The motor consequences include: large angle esotropia (greater than 15°) in 90% of cases (10% of exotropia), a fixation in adduction (or cross-fixation), the presence of a manifest latent nystagmus (40% of cases), a dissociated vertical deviation (50-90% of cases) and an elevation in adduction (hyperaction of the inferior oblique muscle in 70% of cases).

Management of early strabismus

□ **Refraction**

Measuring the objective refraction under cycloplegic conditions is essential in the management of all types of strabismus. In early strabismus, the accommodative factor is possible but inconsistent. Prescribing total optical correction is always indicated.

□ **Amblyopia**

An alternate occlusion (sticky patch occlusion) is often indicated to promote an alternation. Binasal sectors are sometimes proposed to limit the fixation in adduction. Treatment modalities for amblyopia in early strabismus are conventional and based on occlusion or penalization.

□ **Surgical management**

The decision for early surgical management (in the first year of life) has been gradually accepted. Surgery aims at removing or maximally limiting the deviation to restore a potential binocular function. Two options are currently being discussed in the literature: conventional oculomotor surgery or injection of botulinum toxin into the medial rectus muscles.

○ *"Conventional" surgery*

Depending on the operator choice, the technique may associate biocular surgery (weakening of both medial rectus muscles) or bimuscle monocular surgery (weakening of the medial rectus muscle, strengthening of the lateral rectus muscle). This procedure is performed under general anesthesia.

The main risk is the development of comitant strabismus, because studies have shown a spontaneous resolution (partial or complete) of strabismus in 20-30% of cases. A second surgery is thus common and complicated by the cicatricial fibrosis induced by the first surgical procedure. Studies have also shown that early surgery (before the age of two years) was associated with a greater number of re-operations over the lifetime (Simonsz HJ, Kolling GH. Eur J Paediatr Neurol

2011), without providing competitive advantages (deviation and as well binocular vision) compared to late surgery (around the age of 4 years) (Kolling GH, Simons HJ, Haag U, Dinkel H. Strabismus 1997).

○ ***Botulinum toxin***

Botulinum toxin is used in early strabismus since the 1990s. The technique consists in injecting botulinum toxin A into the two medial rectus muscles. This procedure is performed under general anesthesia after opening of the nasal conjunctiva in front of the muscle and injection under visual control. A volume of 0.1 mL containing 5 International Units of botulinum toxin A is generally injected. No botulinum toxin A has to date been premarket-approved for the treatment of early strabismus.

Its advantages include:

- the ability to remove within a few days the spasm in the medial rectus muscles;
- its administration under very short general anesthesia. Its action is limited in time, which limits the risk of consecutive strabismus;
- conjunctival and especially muscle scars are very limited;
- finally, this treatment may relatively easily be repeated in the event of failure.

Studies have shown a success rate ranging between 45% (de Alba Campomanes AG, Binembaum G, Campomanes Eguiarte G. JAAPOS 2010) and 85% (Hautviller V et al. Binocul Vis Strabismus Q 2007; Thouvenin D, Lesage-Beaudon C, Arné JL. JFO 2008; Baggesen K et al. Acta Ophthalmologica 2011) with 1-3 injections of botulinum toxin A.

The described adverse reactions include:

- a divergent strabismus. This is a desired effect since it confirms the efficacy of the injection,
- a transient ptosis (appearing within 3-8 days and lasting up to three months). It is present in more than half of cases, and requires monitoring of the risk of amblyopia;
- rare cases of eyeball perforation, scleritis or mydriasis have been reported in the literature.

○ **What treatment to choose between botulinum toxin and conventional surgery?**

The most frequently used approach of French strabismologists is the use of botulinum toxin A as a first-line treatment in early strabismus. Botulinum toxin should theoretically be injected as early as possible in the child's life to increase the chances of binocular reassociation (Campos EC, Schiavi C et al. J Pediatr Ophthalmol Strabismus 2000). In practice, it may be proposed during the two first years of life, allowing in many cases:

- Decreasing the angle deviation (McNeer KW, Tucker MG, Spencer RF. Arch Ophthalmol 1997; de Alba Campomanes AG, Binembaum G, Campomanes Eguiarte G. JAAPOS 2010);
- Decreasing the rate of re-operation (Thouvenin D, Lesage-Beaudon C, Arné JL. JFO 2008)
- Avoiding early surgery (Gursoy H, Basmak H, Sahin A et al. JAAPOS 2012)

III. Botulinum toxin A and other types of strabismus

The use of botulinum toxin in the other types of strabismus has not formally established proof of its efficacy, and remains a specialist decision.

- Its ease of administration in adults (local anesthesia) and reversible effects may lead to its proposition in some types of strabismus in elderly subjects for whom the risk of anesthesia could discourage the surgical indication (Bansal S, Khan I, Marsh IB. *Strabismus* 2008).
- Some teams also use it in multi-operated strabismus to achieve angle reduction and repeated injections are needed (Hancox J, Sharma S et al. *Br J Ophthalmol* 2012).
- It may sometimes be discussed in children with acute strabismus with a potential for binocular recovery (Jones A, Jain S. *JAAPOS* 2014).