PERISTENT CORNEAL DEFECTS TREATED WITH BOTULINUM TOxin-INDUCED PTOSIS

PTOSIS INDUCIDA POR TOXINA BOTULÍNICA COMO TRATAMIENTO DE LOS DEFECTOS CORNEALES PERSISTENTES

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ABSTRACT

Objectives: To evaluate the use of botulinum toxin (BTX) induced ptosis in the treatment of corneal pathology.

Methods: We employed two BTX injections into the superior lid of 10 eyes (9 patients). We evaluated the degree of ptosis, its duration and the effect on the corneal lesion.

Results: Complete ptosis resulted in seven eyes and the corneal pathology resolved in all of them. There were no relevant complications.

Conclusions: BTX treatment is a simple and safe technique for treating refractory corneal pathology. It has significant advantages over surgical tarsorrhaphy and is especially useful where the pathology does not require surgery (Arch Soc Esp Oftalmol 2007; 82: 547-550).

Key words: Tarsorrhaphy, botulinum toxin, ptosis, persistent corneal defect, contact lens, autologous serum.

RESUMEN

Objetivos: Evaluar el uso de la ptosis inducida mediante toxina botulínica (BTX) en el tratamiento de patología corneal.

Métodos: Se emplearon dos inyecciones de BTX sobre el párpado superior de diez ojos (nueve pacientes). Se estudió el grado de ptosis, su duración y la evolución de la lesión corneal.

Resultados: Conseguiamos la ptosis completa en siete ojos y la resolución de la patología corneal también en siete ojos. No hubo complicaciones importantes con el tratamiento.

Conclusiones: Esta es una técnica sencilla y segura para tratar a pacientes con patología corneal refractaria. Ofrece importantes ventajas sobre la tarsofrafía quirúrgica. Es además especialmente útil en pacientes que por diversas razones no puedan someterse a cirugía.

Palabras clave: Tarsorrhafía, toxina botulínica, ptosis, defecto corneal persistente, lentes de contacto, suero autólogo.
INTRODUCTION

Botulinum toxin type A (BTX) is one of the various toxins produced by clostridium botulinum. The marketed toxin is purified and comprised of two polypeptide chains linked by a disulfide bridge: chain H (85-105 kDa) and chain L (50-59kDa) the latter associated to an atom of Zn. It acts by inhibiting the release of acetylcholine in the presynaptic part of the motor end-plate, producing functional and reversible disenervation of the muscle affected (1).

Alan B. Scott was a pioneer in the use of BTX A as an alternative to strabismus surgery (2). Since then, its use has been extended for the treatment of neuromuscular conditions such as blepharospasm, hemifacial spasm, cervical dystonia, achalasia, etc. (3) and also for various ophthalmological problems, especially in the field of oculoplastics (4).

Persistent corneal defects are a source of high ocular morbidity. Delayed cicatrization, a tendency towards infection and corneal thinning, comprise a significant risk of perforation and permanent visual loss. The techniques used to favor corneal reepithelialization, after failure of the maximum medical treatment, include use of contact lenses and surgical tarsorrhaphy (5,6). Therapeutic contact lenses entail a high risk of infection. Surgical tarsorrhaphy hinders lesion follow-up as well as altering palpebral margins when reverted.

In this study our aim was to assess the efficacy of palpebral ptosis induced by BTX type A as a coadjuvant treatment of persistent corneal defects, in patients with a bad general condition not eligible for surgery.

SUBJECTS, MATERIAL AND METHOD

We conducted a descriptive study of a series of clinical cases of patients with persistent corneal defects. In all cases we indicated surgical tarsorrhaphy, but given their general condition, we considered the option of chemical tarsorrhaphy.

Subjects

The study included nine patients, with a total of 10 eyes, presenting persistent corneal defects, refractory to maximum medical treatment during a period of at least three weeks. This medical treatment included corneal lubrication and autologous serum. Four patients had undergone amniotic membrane transplant, which had also failed. We considered chemical tarsorrhaphy with BTX type A. Informed consent forms were delivered and explained.

The exclusion criteria were:

- Neuromuscular junction disorders: myasthenia gravis, amyotrophic lateral sclerosis, myopathy.
- Drug interactions that enhance the effect of BTX A: aminoglycoside antibiotics, spectinomycin and muscle relaxants such as tubocurarine.
- Patients were examined at the ophthalmology unit of our site during the period from February 2004 to September 2005.

Material and methods

We used BTX type A (BOTOX®; Allergan, Inc). Each vial contained 100 IU of BTX type A, which were reconstituted in 2 ml of saline solution, so that 0.1 ml of reconstituted solution contained 5 IU of BOTOX.

We injected 1.5 ml of the solution (7.5 IU BOTOX) subcutaneously in the medial area and the lateral area of the upper border of the superior tarsal plate. We used an insulin syringe and a 30G needle (fig. 1).

We classified the level of ptosis as complete when there was total palpebral closure; efficient partial when the palpebral closure was not complete but the corneal defect was entirely covered and inefficient partial when there was no complete occlusion of the corneal defect.
Patients were examined the following day and subsequently daily until efficient ptosis was achieved, and thereafter weekly. At each visit we assessed the level of ptosis and evolution of the corneal lesion, conducting photographic controls prior to instillation of fluorescein (fig. 2). We maintained lubricating treatment in all cases. In those patients where ptosis duration was insufficient we repeated the injections.

RESULTS

Our study included nine patients, with a total of 10 eyes, presenting corneal defects refractory to medical treatment. The duration of the defect was at least 3 weeks in all cases.

Five of the patients presented neurotrophic ulcers, two patients corneal defects as a result of microbial infection, one patient (two eyes) keratopathy due to exposure and one patient limbic insufficiency due to the use of mitomycin C in trabeculectomy (table I).

All patients had been treated previously with lubricating ointments. Six of the patients had also received autologous serum, and four were treated with amniotic membrane transplant (table I).

In all cases the appearance of ptosis took place between the second and the sixth day after the injection with BTX (table II). Average duration of ptosis was 40.6 days with a standard deviation of 27.5 days (range 29-56). The patient suffering from limbic insufficiency required repeated treatment after one month, using the same dose. Patients continued with medical treatment during this time.

Resolution of the corneal lesion was achieved in seven eyes in an average period of 42.71 days (range 5-61). One patient, with bilateral disease, died before the last check-up. In the patient with limbic insufficiency due to the use of mitomycin C in trabeculectomy (table I).

Table I.

<table>
<thead>
<tr>
<th>Diagnostic</th>
<th>Previous treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neotrophic ulcer</td>
<td>Lubrication</td>
<td>Terminal neoplasia</td>
</tr>
<tr>
<td>Neotrophic ulcer</td>
<td>Lubrication + autologous serum</td>
<td></td>
</tr>
<tr>
<td>Neotrophic ulcer</td>
<td>Lubrication + autologous serum + AM</td>
<td>AM: Amniotic membrane.</td>
</tr>
<tr>
<td>Neotrophic ulcer</td>
<td>Lubrication + autologous serum + AM</td>
<td>AM: Amniotic membrane.</td>
</tr>
<tr>
<td>Keratopathy due to exposure</td>
<td>Lubrication</td>
<td>Senile dementia</td>
</tr>
<tr>
<td>Bacterial ulcer secondary defect</td>
<td>Lubrication + autologous serum + AM</td>
<td>AM: Amniotic membrane.</td>
</tr>
<tr>
<td>Bacterial ulcer secondary defect</td>
<td>Lubrication + autologous serum + AM</td>
<td>AM: Amniotic membrane.</td>
</tr>
<tr>
<td>Mytomycine C limbic insufficiency</td>
<td>Lubrication + autologous serum + AM</td>
<td>AM: Amniotic membrane.</td>
</tr>
</tbody>
</table>

Table II.

<table>
<thead>
<tr>
<th>Diagnostic</th>
<th>Ptosis</th>
<th>Establishment time</th>
<th>Duration</th>
<th>Resolution of the ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neotrophic ulcer</td>
<td>Complete</td>
<td>5 days</td>
<td>40 days</td>
<td>45 days</td>
</tr>
<tr>
<td>Neotrophic ulcer</td>
<td>Complete</td>
<td>4 days</td>
<td>45 days</td>
<td>50 days</td>
</tr>
<tr>
<td>Neotrophic ulcer</td>
<td>Complete</td>
<td>3 days</td>
<td>37 days</td>
<td>45 days</td>
</tr>
<tr>
<td>Neotrophic ulcer</td>
<td>Partial</td>
<td>6 days</td>
<td>56 days</td>
<td>61 days</td>
</tr>
<tr>
<td>Neotrophic ulcer due to exposure</td>
<td>Complete</td>
<td>5 days</td>
<td>29 days</td>
<td>33 days</td>
</tr>
<tr>
<td>Keratopathy due to exposure</td>
<td>Complete bilateral</td>
<td>2 days RE?</td>
<td>At least 1 month</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 days LE?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial ulcer secondary defect</td>
<td>Partial</td>
<td>4 days</td>
<td>51 days</td>
<td>60 days</td>
</tr>
<tr>
<td>Bacterial ulcer secondary defect</td>
<td>Complete</td>
<td>5 days</td>
<td>42 days</td>
<td>5 days</td>
</tr>
<tr>
<td>Limbic insufficiency. MMC</td>
<td>Partial (retreated)</td>
<td>4 days</td>
<td>25 days</td>
<td>No objective healing</td>
</tr>
</tbody>
</table>

MMC: mitomicina C.
insufficiency due to the use of mitomycin C the treatment was not efficacious, as the corneal defect persisted despite repeated treatment and maximum lubrication (table II).

No patient suffered any complications.

DISCUSSION

All the patients included in our study presented corneal defects refractory to maximum medical treatment and a poor general condition and/or a low level of collaboration. Therapeutic measures included lubrication, autologous serum and amniotic membrane transplant. The use of BTX in these patients to induce protective ptosis was efficacious in seven of the 10 eyes.

In our study, BTX helped to resolve the corneal lesion in patients with neurotrophic ulcers and resulting from bacterial infection. Results were not conclusive in the patient with keratopathy due to his death. In the patient presenting limbic insufficiency, treatment was not efficacious despite repeated treatment.

BTX A acts by diminishing rubbing of the upper eyelid, especially the free border, on the corneal defect, favoring cicatrization (7). This is probably not the only mechanism of action. Several theories have been advanced, on the one hand a decrease in tear evaporation would improve lubrication of the ocular surface, on the other, release of growth factors and cytokines from tarsal conjunctiva would enhance epithelial cicatrization given that ptosis is very proximal to the corneal defect (8).

Other measures that manage to diminish rubbing have some disadvantages. The use of therapeutic contact lenses has been associated to a high risk of microbial infection (5). Surgical tarsorrhaphy produces anatomical alterations on the palpebral border when reverted, such as scar entropion and distichiasis, as well as hindering lesion follow-up (6). In chemical tarsorrhaphy we can examine the cornea perfectly with a slit lamp by manually lifting upper eyelid, which is a clear advantage.

Kirkeness et al (7) considered the possibility that ptosis induced by BTX A favored eye infections by producing tear stagnation. It is difficult to assess this risk with the cases described in literature, which on the other hand, can also occur with the use of therapeutic contact lenses and surgical tarsorrhaphy.

In other series published in literature, BTX has been used injected directly into the center of the elevating muscle of the upper eyelid (7-9) to induce protective ptosis. Kirkness et al. (7,9) in a series of 25 patients, communicated dyplopia in 12% and resolution of the corneal defect in 90%. Ellis and Daniell (8), on the other hand, studied 21 patients, in which 24% had dyplopia and the corneal defect was resolved in 66%. Our results are comparable to those of these series. In any case, our technique differs from the one used by these authors, as we did not cross the orbital septum, which would explain why we had no cases of dyplopia.

Given that the etiology of persistent corneal defects is very diverse, it is difficult to conduct comparative studies between the various therapeutic alternatives, but in any case, the results have been very good.

We consider our technique is efficacious as coadjuvant therapy in the treatment of persistent corneal defects, and it allows following the evolution of the lesion at all times. Given its simplicity, it is especially useful in patients with a poor general condition or limited collaboration.

REFERENCES