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ORIGINAL COMMUNICATION

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Botulinum toxin is effective and safe for palatal tremor

A report of five cases and a review of the literature

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Abstract Palatal tremor (formerly palatal myoclonus) is an extremely rare, but potentially treatable cause, of objective tinnitus. The tinnitus is thought to be secondary to rhythmic involuntary movements of the soft palate. Its aetiology is variable and it remains difficult to treat. Many different medical and surgical remedies have been tried but none have demonstrated reproducible success. Botulinum toxin has been used in sporadic cases and seems to produce good results. Ten patients with palatal tremor have presented to this department over the last three years. After discussion with the patients with regard to the management of this condition and possible complications, five opted for botulinum toxin therapy and five declined further intervention. Clinical diagnosis was made on the confirmation of soft palate movements synchronous with an audible clicking noise. Five patients underwent botulinum toxin injection into the insertion of the levator and tensor veli palatini muscles. Of the five that were treated with toxin, four showed complete resolution of symptoms after a course of treatment. Only one patient reported transient side effects. This would suggest that botulinum toxin is a safe and effective first line treatment for palatal tremor.

Key words palatal tremor · palatal myoclonus · botulinum toxin

Introduction

Palatal tremor is a rare condition first described in 1878 by Politzer [1]. Two discrete variations of the condition have been identified, namely an 'essential' form in which no structural lesion is discernable and a 'symptomatic form' which develops secondary to brainstem or cerebellar disease [2]. Objective tinnitus is a more prominent feature of essential palatal tremor than symptomatic palatal tremor and often presents to otolaryngologists rather than neurologists. Various medical and surgical treatment strategies have been proposed. Medical treatment is based on anti-convulsants and sedatives but no drug has been shown to significantly improve symptoms reproducibly. Surgical procedures also vary and again treatment response is variable with risk of significant side effects. There are a number of sporadic cases reported in the literature where botulinum toxin has been used as a second or third line therapy with good symptom control and relatively few reported side effects [3]. We suggest that botulinum toxin is safe and effective first line treatment in the majority of cases.

Materials and methods

In the last three years ten patients with palatal tremor have been managed in the University Department of Otolaryngology at the Man-

chester Royal Infirmary. To our knowledge this is the largest single unit series reported in the literature.

All ten patients presented with objective, intrusive clicking tinnitus. On examination palatal tremor was observed in all the patients either orally or nasendoscopically. The frequency of ear clicks varied from 60/minute to 120/minute. All patients underwent full audiological assessment to exclude a middle ear cause for the tinnitus. They also underwent magnetic resonance imaging of the brain and brain stem to ensure there was no intrinsic neurological pathology. All investigations were normal in the ten patients. None of the patients had any associated neurological symptoms to suggest that they had symptomatic rather than essential palatal tremor.

Patients were counselled about the use of botulinum toxin including the possibility of limited short-lived side effects. These are usually minor and limited to transient weakness of muscles affected by local spread of the toxin, such as voice change and nasopharyngeal regurgitation [3]. Five patients elected to be treated, one is considering treatment and the other four elected to wait and see if their tinnitus became too intrusive. Those who declined treatment stated that they felt that their symptoms were not especially intrusive and were therefore given the option of re-contacting the department as necessary.

In all cases Botulinum Toxin A (Dysport) was injected into the soft palate posteromedially to the maxillary tuberosity at the insertion of both tensor veli palatini and levator veli palatini [3]. A starting dose of 5 units to the affected side was used in the first case but it became apparent that a greater starting dose of up to 15 units could be used with better symptomatic control.

Results

Five patients elected to undergo botulinum toxin injection to the soft palate after being fully informed of the risks and possible benefits. One patient reported complete resolution of symptoms after the first injection. A further three patients experienced partial symptomatic improvement after the first injection with subsequent complete resolution after a second injection. Symptomatic resolution was sustained for between two and six months. The remaining patient reported only moderate symptomatic improvement and further dose titration is ongoing.

Only one patient reported side effects of difficulty in swallowing, plummy voice quality and velopharyngeal insufficiency. One patient required the primary injection under general anaesthesia. However, all other treatments were administered under local anaesthetic in the outpatients department. No spontaneous improvement has been noted in any of the patients who did not receive the toxin.

Detailed results of the individual patient doses and responses can be seen at the bottom of Table 1.

Discussion

Palatal tremor is a distressing problem, not only for the patients but also in a social context as it is often easily audible. As stated previously two distinct subtypes are recognised. Ear clicks in the absence of other neurological abnormality, as seen in essential palatal tremor, are usually seen in the otolaryngology clinic. Symptomatic palatal tremor is more likely to have associated symptoms and so presents to neurology colleagues.

The aetiology of symptomatic palatal myoclonus is well defined. In contrast, essential palatal myoclonus has no identifiable underlying abnormality. It occurs in isolation and is localised to the soft palate. The main muscle involved is the tensor veli palatini, which originates from the greater wing of the sphenoid, adjoining petrosphenoid fissure and lateral wall of the Eustachian tube. Its tendon joins the palatal aponeurosis within the soft palate [4]. There is some debate as to whether the clicking noise is produced by the walls of the Eustachian tube snapping together [5], or whether separation of the tubal walls with the breaking of surface tension produces it [6]. Sonotubometry and electromyography have failed to confirm either of these possibilities [7]. Palatal tremor is occasionally temporarily suppressed by mouth opening, yawning, swallowing or retching [8]. It is generally considered to be a lifelong disorder although one or two cases of spontaneous remission have been reported [9, 10]. Palatal tremor must be distinguished from middle ear myoclonus as a cause of objective tinnitus. In middle ear myoclonus palatal tremor is not observed but tympanic membrane movement synchronous with the "ear clicks" may be evident. Middle ear myoclonus is more often unilateral and can be relieved by tympanotomy and section of the stapedial and tensor tympani muscles [11].

Treatment is based on anticonvulsants and sedatives but all with very little effect apart from sporadic case reports. No medication has proven to be reliably effective at treating the myoclonus. Likewise surgery has not provided reliable results. Reports of the use of botulinum toxin are increasingly prevalent, but as yet these are again limited to one or two cases treated on single occasions with no long-term follow-up.

The toxin is a potent neurotoxin, which inhibits calcium-mediated release of acetylcholine into the synaptic junction resulting in local chemical denervation and loss of neuronal activity in the targeted organ [12]. This leads to selective muscle paralysis if given locally but the effect is fatal if systemic exposure is sustained. The blockade of the neuromuscular junctions begins to wear off after about twenty-eight days and that is why repeated injections are often necessary. The dose can be titrated to side effects, as the level at which these occur is variable from patient to patient.

Botulinum toxin is not a new treatment for palatal tremor. It became recognised as a potential treatment in the 1990s based on a number of anecdotal case reports. Table 1 summarises the previous reported cases in the English language literature. When considered in conjunction with the authors' series of five cases it can be seen that botulinum toxin should not be reserved for re-

Table 1

Patient [Ref.]	Duration	Main Sx	Dose	Sx Relief	Effect duration	Side effects
52 M [14]	1 year	Rt CT, Lt CT unmasked after right treated	8 U[c], Rt TVP 17 U[c], Rt TVP 17 U[c], Lt TVP	Minimal Resolved Resolved	3/52 3/12 3/12	Nil Initial mild VPI Nil
25 M [3]	NR	Bil CT	5 U[b], Bil TVP	Resolved	12/52	Nil
64 F [3]	12 years	Bil CT	5 U[b], Bil TVP 5 U[b], Bil TVP 5 U[b], Bil TVP 10 U[b], Bil TVP 10 U[b], Bil TVP	Resolved Resolved Resolved Minimal Improved	Few hours Few hours Few hours NR NR	Nil Nil Nil Severe VPI 1/12 Nil
70 F [3]	7 years	Bil CT	10 U[b], Bil TVP	Resolved	1 years	Initial mild VPI
NR [15]	NR	CT	NR[a], TVP	Improved	NR	NR
59 F [16]	8 years	Bil CT	2.5 U[c], Bil TVP + 2.5 U[c], Bil LVP	Resolved	7/12	Initial mild VPI
17 F [17]	< 1 year	Lt CT	20 U[b], Lt LVP 24 U[b], Lt LVP	Resolved Resolved	5/52 > 2/52	Nil Nil
32 F [18]	4 years	Bil CT	7.5 U[c], Bil TVP	Left resolved, right improved	3–4/12	Left aural fullness – VT inserted
41 F [18]	18/12 16/12	Lt CT Rt CT	10 U[c], Lt TVP 10 U[c], Rt TVP	Resolved Resolved	2/12	Hyper nasal speech 2/52
12 F [19]	2 years	Lt CT	20 U[a], Lt TVP	Resolved	1 year	Initial mild VPI
21 M [20]	2 years	Bil CT	5 U[a], Bil TVP	Resolved	3/12	Nil
36 M [21]	15 years Lt 7 years right	Bil CT	5 U[c], Bil TVP + LVP	Resolved	1/12	Nil
11 M [22]	NR	Lt CT	30 U[b], Lt LVP 50 U[b], Lt LVP 60 U[b], Lt LVP	Improved Improved Improved	2/12 1/12 NR	Nil Nil Injections stopped due to local discomfort
26 F	1 year	Bil CT	5 U[b], Bil TVP + LVP 4 U[b], Bil TVP + LVP	Improved Improved	6/52 10/52	2/52 mild VPI Nil
42 M	14 years	Bil CT	15 U[b], Bil TVP + LVP	Improved	NR	Nil
41 M	1 year	Bil CT	15 U[b], Bil TVP + LVP 15 U[b], Bil TVP + LVP 15 U[b], Bil TVP + LVP	Improved Improved Improved	5/12 4/12 6/52	Nil Nil Nil
27 F	3 years	Bil CT	15 U[b], Bil TVP + LVP 20 U[b], Bil TVP + LVP	No effect Improved	NR NR	Nil Nil
35 F	2 years	Bil CT	15 U[b], Bil TVP + LVP	Improved	3/12	Nil

M/F Male/Female; *Rt/Lt* Right/Left; *CT* Clicking Tinnitus; *TVP* Tensor veli palatini; *VPI* Velopharyngeal Insufficiency; *NR* Not recorded; *Bil* Bilateral; *LVP* Levator veli palatini; *VT* ventilation tube

All cases used Botulinum toxin A and doses are comparable. a denotes BOTOX® (Allergan), b denotes Dysport (Ipsen) and c is where the manufacturer is unrecorded. The latter five patients are those reported in this series

fractory cases but should be considered to be a safe and effective first line therapy.

Conclusion

Botulinum toxin has been proven to be a safe effective treatment for many neuromuscular disorders. We believe that it should be considered as a first line treatment for patients with palatal tremor as the current evidence suggests it may be the only treatment with reproducible benefit.

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