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ORIGINAL ARTICLE AESTHETIC

Botulinum toxin application to the buccinator muscle in the treatment of facial synkinesis: a prospective cohort study

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Abstract

Background: Synkinesis may develop following facial nerve palsy, impacting quality of life. Botulinum toxin treatment for synkinesis is commonly used, but buccinator muscle injection is less common. We aim to investigate buccinator botulinum toxin for management of synkinesis.

Methods: Patients received botulinum toxin to synkinetic areas (standard botulinum toxin) with physiotherapy. Four months later they were re-treated at the same sites, with addition of buccinator injections. After both treatments, outcomes were measured using the Facial Disability Index and Synkinesis Assessment Questionnaire at baseline and five weeks later (four assessments in total).

Results: Twenty-seven patients were recruited, 25 completing standard botulinum toxin treatment and 20 completing standard and buccinator botulinum toxin. Standard botulinum toxin showed improvements in the Synkinesis Assessment Questionnaire (63.5 v 50.3, $p < 0.001$) and Facial Disability Index–Social (59.2 v 73.8, $p < 0.001$). Further benefits were noted with buccinator botulinum toxin in the Synkinesis Assessment Questionnaire (52.2 to 44.4, $p = 0.017$) and Facial Disability Index–Social (72.6 to 77.4, $p = 0.049$). Synkinesis Assessment Questionnaire subset analysis showed improvement in ocular synkinesis with buccinator botulinum toxin (9.3 to 7.8, $p = 0.04$).

Conclusion: Botulinum toxin treatment with physiotherapy is effective for synkinesis and reducing social impact. Addition of buccinator botulinum toxin resulted in further improvements.

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Introduction

Facial expression is a vital component of social interaction, particularly in communicating emotions.[1,2] Inability to express emotion as a sequelae of facial nerve palsy (FNP) is reported to be the most distressing aspect.[3] Synkinesis is an involuntary facial movement occurring simultaneously with voluntary movement of muscles innervated by the ipsilateral facial nerve.[4] It is found in up to 55 per cent of patients who experienced severe Bell's palsy.[5] Synkinesis further impacts quality of life and complicates emotional expression.[6]

Treatment of synkinesis is complex, with strategies including physiotherapy, botulinum toxin (BTX) and surgical intervention, used on their own or in combination. Surgical interventions include selective neurectomy, selective myectomy and complete facial nerve sacrifice with reconstruction, however all are irreversible.[7–10] Chemodenervation with BTX is also used for control of facial hypertonia, reducing synkinesis and improving facial symmetry.[4,11–15] It is our experience that the combination of physiotherapy and BTX, administered by an experienced practitioner in facial nerve disorders, results in favourable outcomes.[16]

Treating the buccinator muscle with BTX for synkinesis was first reported by Wei and colleagues, who showed significant improvements in quality of life.[17] This was replicated by Patel and colleagues who offered buccinator BTX to patients with oral tightness, showing improvement in selective domains of the Synkinesis Assessment Questionnaire (SAQ),[18] which the authors defined as buccinator specific.[19] The same centre also reported that use of buccinator BTX had increased from 10 per cent to 39 per cent of patients treated with BTX over the last few years.[20]

To date, none of the research methodology was sufficient to elucidate the specific function of buccinator BTX injection. We aim to define the role of buccinator muscle BTX in the management of facial synkinesis with a crossover design.

Methods

This was a single arm prospective study with internal controls. Patients were recruited through the Sydney Facial Nerve Service (SFNS) from October 2019 to June 2020. Inclusion criteria were patients with synkinesis following FNP who were recommended to undergo BTX and physiotherapy.

The BTX injection was performed by a single clinician (GH) in clinically affected areas and facial physiotherapy was performed by a specialised physiotherapist (SC). Physiotherapy occurred one week post-injection and home exercises were prescribed for daily routine, with follow-up appointments after each treatment. During assessment, key muscles (frontalis, corrugator, orbicularis oculi, levator labii superioris alaeque nasi, depressor anguli oris, mentalis and platysma) were assessed for power, symmetry and synkinetic movement. Targeted examination of the expected location of the respective muscles was used to identify injection sites. Buccinator synkinesis was assessed by instructing patients to blink and inspecting buccal mucosa while watching for buccinator activation. Low-dose BTX was applied to each of the muscle groups in a single point (2.5–5 units) with the exception of frontalis and corrugator (up to 10 units), and platysma (up to 40 units), with injection in multiple points to cover more of the respective muscles. In all cases, onabotulinum toxin Type A was used with a dilution of 100 units into 2 ml of 0.9 per cent sodium chloride.

Patients were contacted by phone to complete the questionnaires on the day of their first treatment (baseline) and again five weeks later (standard BTX). The treatment and questionnaires were repeated four months later, allowing for a washout period. On the second treatment, the site and dose of BTX injections remained the same, with the addition of 2.5 units of BTX to the ipsilateral buccinator muscle applied through an intraoral approach with the patient's mouth open. Patients were called on the day of their second treatment (washout), as well as five weeks later (standard BTX with buccinator BTX) with questionnaires repeated each time.

Questionnaires administered included the SAQ[18] and the Facial Disability Index (FDI).[21] The SAQ is a validated questionnaire evaluating morbidities relating to synkinesis[18,19] while the FDI is validated for examining the impact of FNP on quality of life. The FDI consists of social (FDI-S) and physical (FDI-P) components.[21]

Ethics approval was granted by Sydney Local Health District Ethics Review Committee (Royal Prince Alfred Zone) with approval X16-0367 and 2019/ETH07164 9.49/OCT20.

Statistical analysis

Statistics were analysed using R x64 v3.5.1 (The R Foundation for Statistical Computing, Vienna, Austria). Mean pre and post scores were compared using paired *t*-tests. Subscore analysis of the SAQ

was performed based on the end organ effect on the ocular region (Q1–3), platysma region (Q4 and 7), face region (Q5, 6 and 9) and tearing (Q8). Statistical significance was defined as a p value < 0.05.

Results

Twenty-seven patients were recruited for this study with a mean age of 47.3 ± 14.7 years. Median duration of FNP was two years, with a range of 0.5 to 21.3 years. Females represented 93 per cent of the cohort (n = 25). The most common cause of FNP was Bell's palsy (70%, n = 19), followed by herpes zoster oticus and post-surgical causes (11% each, n = 3) (**Table 1**).

Table 1. Demographic and patient-related data

Characteristic	Value
All patients (n)	27
Age (years): mean (SD)	47.3 (14.7)
Female: n (%)	25 (93)
Male: n (%)	2 (7)
Aetiology	**N (%)**
Bell's palsy	19 (70)
Herpes zoster oticus	3 (11)
Other	2 (7)
Post-surgical	3 (11)
– Meningioma	1
– Paraganglioma	1
– Acoustic neuroma	1

SD = standard deviation

The median total dose of BTX used per patient was 25 units (range 10–40 units). The most variable site was the platysma, with doses ranging from 10 to 40 units. The most commonly injected muscle was the depressor anguli oris (67%, n = 18). The least injected muscle was the frontalis (15%, n = 4) (**Figure 1**).

Twenty-five of the 27 patients completed the first treatment assessment (baseline and standard BTX), and 20 completed the second treatment assessment (washout and standard BTX with buccinator BTX). Two patients who dropped out between the first injection and repeat injection described over-flaccidity of their face, relating it to feeling that their original palsy had recurred. Reported benefits from patients included generally an improved feeling of 'tightness' in their face post the buccinator BTX (n = 14, 70%). Three of the 20 patients (15%) reported weakness in their cheek with some ballooning during speaking.

Significant improvements in SAQ were observed following standard BTX, from 63.5 at baseline to 50.3 (mean difference 13.2, 95% confidence interval (CI) 7.4–18.95, $p < 0.001$). Mean SAQ score deteriorated during the washout period to 52.2 ($p = 0.048$) and repeat injection (standard BTX with buccinator BTX) improved mean SAQ score to 44.4 (mean difference 7.8, 95% CI 1.5–14.0, $p = 0.017$) (**Table 2**). There were significant improvements in FDI-S from 59.2 to 73.8 (mean difference 14.6, 95% CI 6.5 to 22.5, $p < 0.001$) for standard BTX and significant improvements for standard BTX

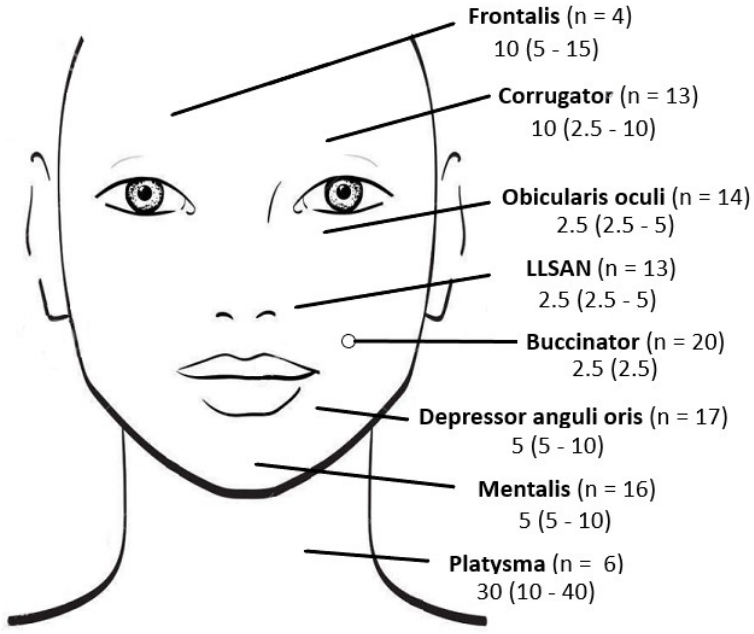

Fig 1. Botulinum toxin injection map in median units (range)

LLSAN = levator labii superioris alaeque nasi

Table 2. Pre- and post-treatment scoring between standard botulinum toxin and buccinator-inclusive botulinum toxin

Scores		Baseline	Standard BTX	Washout	Standard BTX with buccinator BTX
SAQ	**Mean (SEM)**	63.5 (3.4)	50.3 (2.7)	52.2 (2.5)	44.4 (2.7)
	***p*-value**	–	< 0.001†	0.006‡	0.017§
FDI-P	**Mean (SEM)**	66.4 (3.8)	68.4 (2.3)	73.3 (2.7)	75.5 (2.3)
	***p*-value**	–	0.63†	0.23‡	0.35§
FDI-S	**Mean (SEM)**	59.2 (4.2)	73.8 (2.6)	72.6 (3.6)	77.4 (2.7)
	***p*-value**	–	< 0.001†	0.006‡	0.049§

SAQ = Synkinesis Assessment Questionnaire; SEM = standard error of the mean; FDI-P/S = Facial Disability Index physical/social; BTX = botulinum toxin; † = paired t-test between baseline and standard BTX; ‡ baseline and washout; § washout and standard BTX with buccinator BTX

Fig 2. Effects of buccinator-inclusive botulinum toxin. Baseline clinical photography showing (A) at rest and (B) oculo-oral synkinesis. The same patient one month post repeat botulinum toxin injections including buccinator (C) at rest and (D) showing reduction in oculo-oral synkinesis

with buccinator BTX from 72.6 to 77.4 (mean difference 2.3, 95% CI 0.03–9.6, $p = 0.049$). There was no significant change during washout from 73.8 to 72.6 (mean difference 1.2, $p = 0.44$). The FDI-S and SAQ were significantly improved when comparing washout to baseline ($p = 0.006$ for both). The FDI-P did not change significantly between any time points, from baseline score at 66.4 to 68.4 post standard BTX ($p = 0.63$), to 73.3 during washout ($p = 0.23$) and to 75.5 post standard BTX with buccinator BTX ($p = 0.35$) (**Table 2**). Before and after photographs of clinical effect are demonstrated in **Figure 2**, showing noted benefits in resting symmetry, particularly around the

ipsilateral eye, and significant improvements in oro-ocular synkinesis on active movements. These improvements were commonly noted post repeat injections with buccinator BTX.

Subscore analysis on the SAQ questionnaires demonstrated that application of BTX improved all domains significantly within the SAQ; however, standard BTX with buccinator BTX resulted in additional significant improvement in ocular synkinesis subsets alone (7.8 from 9.3, $p = 0.04$) (**Figure 3**).

Discussion

This study demonstrated significant improvements in social function and synkinesis following standard BTX and physiotherapy among patients with FNP. It also showed further improvements with repeated BTX injections including buccinator BTX, especially in ocular-related symptoms. These results reinforce the effectiveness of facial physiotherapy and standard BTX therapy, as well as the benefits of repeated BTX with buccinator treatment.

Patel and colleagues postulated that buccinator holds significant bulk in the midface; with its proximity to multiple branches of the facial nerve increasing risk of aberrant facial nerve connection leading to synkinesis.[19] As oral-ocular synkinesis is the most common location of synkinesis (up to 89%),[22] the buccinator as a historically overlooked and undertreated site likely explains the subscore benefit in ocular movements over other areas.

The BTX doses used in this study (median 25 units) were considerably lower than that reported by Wei and colleagues (median 54 units) in the original paper highlighting buccinator BTX effectiveness.[17] They also used an adjustable buccinator dosing of 0.6–2.5 units, compared to our standard 2.5 units, which is similar to the dose reported by Patel and colleagues,[19] though they have recently increased the dose to 5.0 units.[20] It is our experience that 2.5 units was adequate for clinical effect, allowing for subsequent dose increase if required, and avoiding over flaccidity on first injection (as mentioned by two patients who withdrew from the study as well as three patients post-buccinator BTX). Wei and colleagues also reported cheek flaccidity as a potential side effect in their cohort. No patients in our or previous literature reported mastication concerns.

Females made up the majority (87%) of patients recruited. While there are no known gender differences in the rates of FNP, this is representative of the demographics for patients seen at our clinic.[23] The most common aetiology of Bell's palsy is also representative of our clinic population.[16]

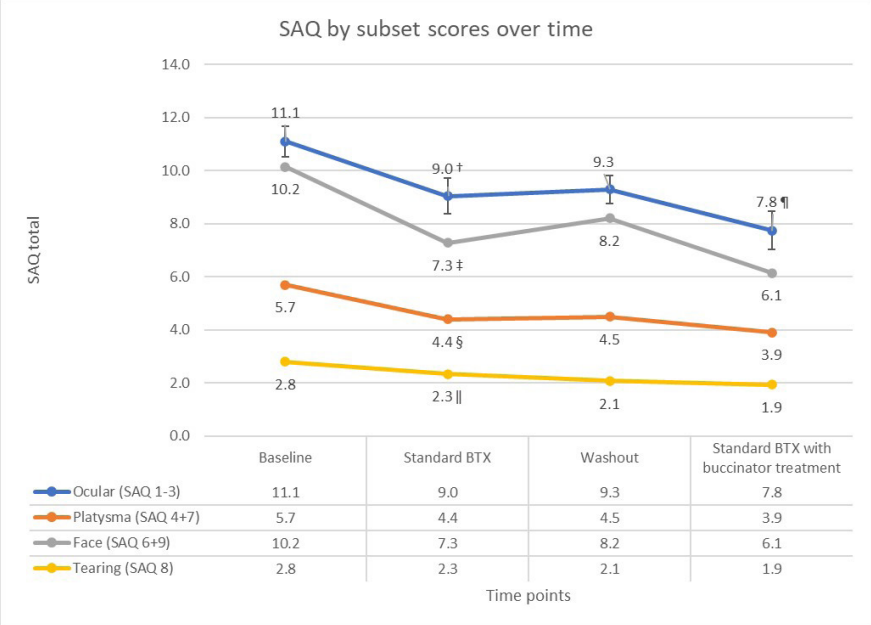

Fig 3. Synkinesis Assessment Questionnaire subsets over time with standard BTX and standard BTX with buccinator BTX. All p-values from paired t-tests:
† p-value = 0.04, between baseline and standard BTX for ocular subset
‡ p-value = 0.01, between baseline and standard BTX for face subset
§ p-value = 0.04, between baseline and standard BTX for platysma subset
‖ p-value = 0.03, between baseline and standard BTX for tearing subset
¶ p-value = 0.04, between washout and BTX with buccinator injection for ocular subset

SAQ = Synkinesis Assessment Questionnaire; BTX = botulinum toxin

The pharmacological and clinical effects of BTX usually last about three months, but this is highly variable and effects may last up to six months in some patients.[24] For this study, we allowed for a washout period of four months prior to the second injection. Interestingly, we note that the SAQ and FDI-S scores were significantly better prior to the second injection as compared to baseline. This may be due to the benefits of facial physiotherapy with cortical adaptation or inadequate washout of BTX that could be experienced by some patients. Patients may also have a better outlook on their facial function based on recent improvements from the first injection, resulting in better self-reported outcomes.

Limitations

The overall number of patients recruited was small which might carry risk of type I error. Dropouts may have led to attrition bias, where those who felt they were receiving benefit may have continued to respond. The effect of repeated injections may be additive and specifying buccinator addition as the cause for further improvement may be incorrectly implicated when compared to the effect of additional treatment with physiotherapy.

Conclusion

Standard BTX in combination with facial physiotherapy is an effective therapy for the treatment of facial hyperkinesis and synkinesis. The addition of buccinator in BTX therapy further improves the management of synkinesis and quality of life of patients with facial synkinesis.

Patient consent

Patients/guardians have given informed consent to the publication of images and/or data.

Conflict of interest

The authors have no conflicts of interest to disclose.

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