study child was submitted. In this study, wheeze was observed for an average of 1.1 days of every 10.4 days of rhinovirus episodes. So, within the maximum 2.3 days available for symptom reduction, we would not expect prevention of more than 0.24 days per child of wheezing throughout the six months of the study.

Viruses were cultured in only 22.2% of medicable and 23.8% of non-medicable episodes in this study. This viral isolation rate is comparable to the viral yield in the earlier adult study. We do not know the contribution of coronaviruses to the present cases as they were not assessed serologically, but our adult studies suggested that contact prophylaxis was ineffective in preventing coronavirus infections.

We conclude that the contact prophylaxis approach in these high-risk children does not offer theoretical benefits. Our observations show that these young school-age children are more often than not the initiators of respiratory episodes within their families and therefore at these times would be unable to make use of contact prophylaxis. Further, it would seem that while they experience

possibly preventable rhinovirus-associated illness, this infection is not associated with substantial lower respiratory symptomatology and that for them the cost of the intranasal medication would be relatively unlikely to be balanced by clinically appreciable benefits.

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Treatment of idiopathic spasmodic torticollis with botulinum-A toxin: a pilot study of 19 patients

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ABSTRACT Nineteen patients with spasmodic torticollis, unresponsive to standard therapy, were administered local injections of botulinum-A toxin into the affected muscles. During an average follow-up period of 11.5 months, a more than 25% improvement was noted in 14 of 19 patients. All those with purely focal dystonia and 9 of 10 patients with a disease history of less than three years benefited from treatment. Side effects were insignificant and transient. Botulinum toxin is a very effective and safe method of treatment for spasmodic torticollis. (*Med J Aust* 1990; 152: 528-530)

The term "dystonia" was coined by Oppenheim in 1911¹ in describing six patients with alterations in muscle tone, sustained posturing and involuntary movements. Since then the definition of dystonia has undergone many modifications, and is now described as "a syndrome of sustained muscle contractions, frequently causing twisting and repetitive movements or abnormal postures".²

Dystonia is classified according to age of onset, aetiology (symptomatic or idiopathic) and distribution. Thus, there are focal, segmental and generalized dystonias. Where a single area is involved, such as the eye (blepharospasm), face (oromandibular dystonia), neck (torticollis), or vocal cords (spasmodic dysphonia) the condition is called focal dystonia.² The commonest form of focal dystonia is spasmodic torticollis (ST) with a suggested prevalence of three per 10 000.³ When two or more contiguous parts are involved in the disease process, such as the face and the neck, for example, it is called segmental dystonia, and generalized dystonia when one or both legs and the trunk are affected. Hemidystonia involving half the body usually indicates symptomatic dystonia, with abnormality in the basal ganglia.

Spasmodic torticollis was first described by François Rabelais, the French humanist, author and physician, in the 16th century. The mean age of presentation is 40 to 50 years, and the female to male ratio is 3:2.⁴ Various combinations of neck posture may occur, such as laterocollis, retrocollis and antecollis. The head may be tilted onto one shoulder, and one of the shoulders may be elevated and displaced anteriorly. Intermittent or continuous tremor or spasmodic

movement may occur. The severity of the abnormal postures and movements can be aggravated by stress and an activity such as walking, while improvement may be achieved by the patient touching the chin, face or the back of the head. This is the so-called *geste antagonistique*, quite characteristic of ST but lacking an adequate explanation at the present time. The involuntary movements cease during sleep. Pain can be very severe, intractable and disabling. The onset may be sudden or gradual, the condition usually progressing for a few years and then becoming stationary. Remissions occur in 15% of patients, usually in the first few years after the onset. Many patients are unable to work, and even such activities as driving a car, eating, reading or watching television may become difficult or impossible. The obvious neck deformity causes a constant embarrassment, and the patient's suffering is increased by the lack of understanding and the ineffective therapies available. Medical treatment and psychotherapy are usually unsuccessful.⁵⁻⁷ Surgical treatment may have adverse results,⁸ a significant morbidity and even a small mortality.⁹

Botulinum-A toxin, a neuroparalytic agent, has recently been used in the treatment of focal dystonias. It was pioneered for the treatment of strabismus by Dr Alan Scott¹⁰ and has been shown to be effective for the treatment of blepharospasm,¹¹⁻¹⁴ oromandibular dystonias,¹⁵ spasmodic torticollis,¹⁶⁻²⁰ spasmodic dysphonia²¹ and focal hand dystonias.²² Clostridium botulinum produces eight distinct neurotoxins, which cause widespread muscular paralysis, characteristic of the often fatal syndrome of botulism. When botulinum-A toxin is injected intramuscularly in minute quantities local denervation and muscle weakness occur, lasting for several weeks until the nerve endings regenerate. The toxin inhibits the release of acetylcholine, probably by interfering with calcium channels.²³

Over the past two years we have used botulinum-A toxin to treat over 75 patients suffering from ST. We report the results of a pilot study of the first 19 patients, who have been followed up for an average of 11.5 months.

Patients and methods

Nineteen patients (11 women and 8 men), aged from 30 to 76 years (average, 47.4), were entered in the study. The patients were referred to one of us (I T L) because of ST which was intractable to the usual medical and surgical measures. The duration of the torticollis before our treatment was from 9

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TABLE: Summary of patients treated for spasmodic torticollis with botulinum-A toxin injections

No. of patients	Age (years) Mean (range)	Duration of symptoms Mean (range)	Duration of follow-up Mean (range)	Type of dystonia (n)			Results (n)			
							Improved			75%
				Focal	Segmental	Generalized	25%–50%	50%–75%		
Women 11	47.9 (30–68)	5 years (9 months–15 years)	1 year (6 months–2 years)	6	4	1	1	4	5	1
Men 8	47.1 (32–76)	6 years 9 months (1–18 years)	9.5 months (6–18 months)	—	4	4	2	1	1	4
Total 19	47.4 (30–76)	5 years 11 months (9 months–18 years)	11.5 months (6 months–2 years)	6	8	5	3	5	6	5

months to 18 years (mean, 5 years 11 months). The follow-up ranged from 6 months to 2 years (mean, 11.5 months). Six patients had focal dystonia, eight segmental dystonia, and five generalized dystonia (Table).

All patients had had several unsuccessful trials of medical therapy, physiotherapy and/or psychotherapy. Two patients had undergone accessory nerve section combined with anterior rhizotomies of the C1-C3 nerve roots, and one patient a unilateral thalamotomy, all with disappointing results. The associated conditions were essential tremor in two patients, affective psychosis in two, unilateral blindness in one, bilateral blindness in one, and haemochromatosis in one patient.

After giving informed consent, the patients were offered botulinum toxin treatment. All patients remained ambulant during the therapy and continued to take their previous medications.

Patients were assessed clinically by one of us (I T L) and graded according to the scale of Tsui et al.¹⁷ Pain was graded on a scale of zero to 10. Note was taken of ability to cope with activities of daily living. Videotape recordings of each patient were made before treatment and surface electromyography of the sternomastoid, trapezius and splenius capitis muscles was performed. One week after the injection, patients reported by telephone any side effects, as well as beneficial results. The patients were reviewed at six weeks and 12 weeks after injection and a repeat videotape recording was made. The randomized "before" and "after" videotape recordings were assessed "blind" by two of us (S S and C Y) and graded according to the torticollis scale of Tsui et al.¹⁷ Patients were asked to assess their improvement quantitatively. Particular attention was paid to the amount of pain and to any changes in activities of daily living.

Botulinum-A toxin was obtained from the Smith-Kettlewell Eye Research Institute, San Francisco, USA. The toxin was supplied as a freeze-dried powder, at a temperature of -20°C , in vials containing 100 mouse units (1 mouse unit = 50% lethal dose = 0.4 ng). Immediately before use the toxin was reconstituted with 1 mL of 0.9% saline, without added preservative. One millilitre of the reconstituted toxin contained 100 mouse units.

A tuberculin syringe and a 27 or 25 gauge needle were used to inject up to 50 mouse units of botulinum-A toxin into each of two to three muscles affected by involuntary spasms. The muscles selected were those most affected clinically. The sites usually chosen were the sternomastoid opposite to the direction of rotation of the chin, and the splenius capitis and trapezius muscles ipsilateral to the rotation (Figure). The injection sites were modified according to the clinical picture or the electromyographic findings. Up to 150 mouse units of botulinum toxin were given on the first occasion. Injections were repeated when the clinical effect was wearing off, usually at three-monthly intervals. When the initial effect was unsatisfactory, the dose of toxin was increased by 50%. The maximum given on subsequent occasions was a total of 250 mouse units.

Results

The results are summarized in the Table. An improvement of 25% or more was noted in 14 of the 19 patients (74%), and the remaining five (26%) showed either no change or insignificant improvement. Patients with focal dystonia had the best results, all achieving a more than 25% improvement; patients with generalized dystonia rarely benefited; and the results for those with segmental dystonia fell between these two groups. Female sex, focal dystonia and a duration of disease of less than three years were good prognostic indicators, while male sex, generalized dystonia and chronic disease were unfavourable signs.

Sixteen patients suffered from pain of varying intensity — 12 (80%) obtained relief and in four the pain remained unchanged.

FIGURE: Botulinum toxin injection sites (modified from Tsui et al.¹⁹).

Fourteen patients were better able to cope with activities of daily living: some were able to return to work or resume housework, a few were again able to drive, and most became more mobile and active.

In 12 patients, the side effects consisted of pain at the injection site. The pain lasted 24 to 48 hours and was usually of moderate severity. Muscle weakness around the neck occurred in three patients and transient lethargy for about one to two days was reported in two.

Improvement was never instantaneous, but occurred usually within two to ten days of the injection, reached a maximum in four to six weeks and lasted for nine to eleven weeks. Repeat injections were given at approximately three-monthly intervals. Four patients discontinued treatment, three because of a virtual remission in their symptoms and one because of lack of response.

Clinical records

The following clinical records are fairly typical of the group as a whole.

Case 17

A 32-year-old female secretary developed gradual stiffening as well as twisting and jerking movements of the neck nine months before botulinum toxin treatment. Her neck started to turn to the left and attempts to control it caused pain and a jerking movement. She consulted a number of specialists as well as physiotherapists and practitioners of alternative medicine. She took anti-inflammatory agents, benzhexol, dopa-depleting agents and benzodiazepines, all to no avail, and underwent an intensive course of meditation. She gave up work, became depressed and lost 4 kg of weight.

When seen in June 1987 she had moderately severe torticollis and

some dystonic posturing of the trunk. She was treated with injections of 50 units of botulinum-A toxin in the right sternomastoid muscle and 50 units each into the left trapezius and splenius capitis muscles. Improvement started within one week of treatment and continued for two months, and she has remained well for at least two years. She resumed work and all her usual activities. She is now in remission. It is possible that she is one of the 15% in whom spontaneous remission occurs, but her improvement coincided with the injection of botulinum toxin.

Case 3

A 48-year-old male mechanic suffering from haemochromatosis, which was treated with weekly venesections, developed spasmodic torticollis 18 months before he was referred for botulinum toxin treatment. He saw several neurologists, and other specialists, including a psychiatrist. Anticholinergics, benzodiazepines, haloperidol, tetrabenazine and clobazam were tried without success. When first seen he had violent twisting movements of the neck to the right, associated with rapid jerking of the right shoulder, and spasms of his jaw muscles, with severe pain in the neck and right shoulder. He had to give up work and was hospitalized for two weeks to control his condition, with only partial success. He gave up driving his car. Financial difficulties resulted because of his enforced unemployment and he became depressed.

Injections of botulinum-A toxin into the left sternomastoid, both trapezii and the right splenius capitis muscles were given on three separate occasions over a period of three months. The total amount of botulinum toxin injected was 550 units. Significant improvement occurred, and the patient was able gradually to stop most of his medications and return to casual employment. He still attends for toxin injections every three to four months, and is significantly better than previously.

Discussion

Idiopathic spasmodic torticollis is the commonest form of focal dystonia. A report from Rochester, Minnesota, gave a prevalence rate of 88.6 per million, higher than the prevalence of such neurological diseases as muscular dystrophy and myasthenia gravis.²⁵ Botulinum-A toxin was first used in the treatment of torticollis by Tsui in 1985.¹⁶ Since then several authors have reported favourable results.^{18,19,23.}

We obtained a better than 25% improvement in 14 of our 19 patients (74%), and in 11 the improvement was rated as more than 50% (Table). These results are similar to those of other studies reported. Patients usually obtained better head control, alleviation or relief of pain and significant improvements in ability to cope with activities of daily living. Objective measurements mirrored these subjective reports. Understandably, patients with focal dystonia responded best of all, and those with generalized dystonia had the least satisfactory results: nine of 10 patients with focal dystonia improved, while two of five individuals with generalized dystonia benefited from the treatment. Men responded less well than women. One of the reasons for this difference may be that the relatively larger and stronger muscles of men require higher doses of botulinum toxin to produce a paralysis equivalent to that in women. We now attempt to adjust dosages according to body weight and muscle bulk. In 10 patients the duration of the symptoms was less than three years. Nine of these patients improved. On the other hand, of nine patients whose symptoms had been present for more than three years only five benefited.

We have not come across definite cases of resistance of botulinum toxin, suggesting the possible presence of antibodies. In those cases, however, where an initial good response is followed by unresponsiveness, the search for antibodies may be warranted.

In 80% of cases there was often dramatic relief of pain, even before the muscular overactivity abated and, on a number of occasions when torticollis was successfully relieved, dystonia in other more distant parts of the body also improved. These observations

suggest that botulinum toxin may modify central mechanisms of pain and motor control, perhaps through retrograde transport of the toxin to the motor nerve cell.

It is unlikely that our good results are due entirely to a placebo response, as the results of treatment were often sudden and dramatic, where other modalities, even surgery, had failed. In up to 15% of patients with ST the symptoms may remit in the first five years of the illness, so some cases of improvement may be examples of a natural remission hastened by botulinum toxin injections. We hope to confirm the validity of our present results in the near future with a controlled double-blind trial.

Side effects in this series were minimal; Stell et al. in their recent report mentioned that seven of 10 of their patients developed dysphagia, and took some weeks to recover.¹⁸ This difference in side effects is probably due to the higher dosages employed by the English investigators. When given intramuscularly in appropriate amounts, botulinum toxin appears to be an extremely safe agent. The effects of inadvertently high doses can be potentially reversed by giving intramuscular antitoxin.²⁵

The main disadvantage of botulinum toxin injections is the necessity for repeated injections, given in this series at intervals ranging from one to four months. The injections cause little inconvenience or side effects, and only one patient elected to discontinue treatment on account of lack of response. Three patients were relieved of their symptoms after one to three injections.

At present, botulinum toxin is an investigational agent, released by the manufacturers to certain investigators under specified research protocols. Once the US or British authorities approve its commercial release, it may become more widely available.

Botulinum toxin appears to be the treatment of choice for idiopathic spasmodic torticollis, as well as for an ever increasing number of spasmodic movement disorders.

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