

Commentary

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Being toxic to the oesophagus

Treatment of achalasia is symptomatic. Whether we use pills, intrasphincteric injections, dilating balloons or cutting knives, all we can do to help the patient is to decrease the resistance to forward flow at the cardia, so that swallowed boluses pass more easily into the stomach. As long as we cannot restore oesophageal peristalsis and improve lower oesophageal sphincter (LOS) relaxation, treatment will be limited to prevention of oesophageal stasis which is the cause of most symptoms and complications of achalasia.

Several drugs, particularly long-acting nitrates and calcium channel blockers, have been used to reduce LOS pressure and thus the resistance at the cardia and to relieve symptoms of achalasia. The failure rate due to insufficient potency, side effects or progression of disease is around 50%. These drugs are beneficial only for short term management in patients with relatively mild symptoms or as a temporary measure.¹

A second treatment modality of achalasia is pneumatic dilatation of the cardia. Long term relief of dysphagia (no or occasional dysphagia, once or less than once a week) can be achieved in 75% of patients.² The main disadvantages are the pain of the procedure and the risk of oesophageal perforation, which is usually between 2 and 5%.

Surgical cardiomyotomy yields good results in about 85% of patients. The relatively high incidence of gastro-oesophageal reflux disease after a Heller operation (10-20%) has led most surgeons to combine the myotomy with an antireflux procedure.³ The feasibility of keyhole procedures has been shown, but more experience is needed to make sure that the cost-benefit advantage is not outweighed by the long term results.

Recently, a novel treatment approach has been proposed – the intrasphincteric injection of botulinum toxin during endoscopy.⁴ When injected into the wall of the LOS of patients with achalasia, this potent neurotoxin can reduce LOS pressure sufficiently to improve dysphagia in 90% of patients initially and in 60-66% after six months.^{5,6} The rationale of this treatment is that the toxin binds to the parasympathetic nerve endings in the sphincter and produces a chemical cholinergic denervation of the LOS.

Cuillière *et al*, in this issue (see page 87), report the results of botulinum toxin injection in 55 patients with achalasia who were then followed for six months. This is the first relatively large multicentre study to confirm the original reports on the use of botulinum toxin in the treatment of achalasia. The procedure seems to be safe and to result in notable clinical improvement in 60% of patients at six months, even when it is performed in non-specialist centres. Using 24 hour pH probe studies to evaluate the incidence of gastro-oesophageal reflux, no increased incidence of abnormal acid reflux was observed. An additional strength of the paper is the cautious interpretation of the symptomatic response. A score of ≤ 3 on the Eckardt grading system⁷ is often interpreted as clinical remission. The authors rightly and moderately call it “improvement”.

In 1992 Eckardt *et al*⁷ proposed a grading system for the evaluation of clinical symptoms in achalasia, in which the frequency of three symptoms (dysphagia, regurgitation and pain) is used to produce a score. Depending upon whether any of these symptoms occurred never, occasionally, daily, or with each meal, a symptom score of 0 to 3 is applied. In subsequent papers^{5,6} this type of scoring system was used to classify the clinical outcome of treatment: a score ≤ 3 is interpreted as “remission”. The symptoms on which the score is based are not weighted. The same score is applied to an innocent symptom (mild chest pain) as to regurgitation, which exposes the patient to severe bronchopulmonary complications, and dysphagia, which may make the life of the patient miserable. Applying this scoring system to a patient who has occasional dysphagia, no pain and regurgitation every two or three days, a score of 3 is obtained. Similarly, a patient with daily dysphagia, no pain and occasional regurgitation also has a score of 3. In both instances, treatment would be a success according to this grading system. In other scoring systems such results would have been called “poor”, or a relapse, necessitating another course of treatment.² Perhaps it is time for those interested in the treatment of achalasia to try to reach a consensus grading system, now that a new treatment modality is becoming available.

A limitation of the paper by Cuillière *et al* is the lack of a control group to compare botulinum toxin injections with other treatment modalities. Very recently, Annese *et al*⁵ performed a controlled trial in a small group of patients. Botulinum toxin injections seemed to be as effective as dilatation for the immediate relief of symptoms, but seven of the eight patients in the botulinum toxin group required a second injection because of recurrent dysphagia. Clearly, larger controlled trials are needed using an adequate scoring system for the symptomatic response and precise and clinically meaningful definitions of failure and relapse.

However, before engaging in a large scale, long term trial comparing botulinum toxin with a specific type of pneumatic dilatation or surgical procedure, a dose finding study is essential. Indeed, the greater and longer lasting response rate in the study by Annese *et al*⁵ compared with those of Pasricha *et al*⁶ and Cuillière *et al* may be related to the higher dose of toxin injected (100 units instead of 80) in a wider area of the LOS region in the former study.

LOS pressure after treatment with pneumatic dilatation or botulinum toxin was shown in most large studies to be a good predictor of treatment outcome.⁷⁻⁹ This variable has even been used with success for many years as a guide to determine the number of successive pneumatic dilatations required to achieve optimal results.⁹ In the study by Cuillière *et al*, however, the LOS pressure after botulinum injection did not prove to be a reliable predictor of outcome. It is not clear whether this is due to the techniques of measuring and calculating LOS pressures or to the scoring system used at the different centres.

Botulinum toxin should now be considered as a possible alternative for other accepted treatment modalities – for example, pneumatic dilatation and standard or keyhole surgery. Because of the simplicity and safety of the technique, the procedure may be performed on an ambulatory basis, which would make it an attractive, low cost alternative. Before taking botulinum toxin injections as a valid alternative treatment of achalasia, we need a formal comparative trial of botulinum toxin and pneumatic dilatations as well as more data on the long term efficacy of botulinum toxin. A follow up period of six months to two years is not long for a condition such as achalasia, which is known to deteriorate considerably 10 and 20 years after surgery.¹⁰ One also would want to know whether repeated injections of botulinum toxin will be required and, if so, whether this will be devoid of unwanted side effects, related to the possible transport of the toxin to the spinal cord or brain stem by retrograde axonal migration. It may take several years before these validation studies are completed. At present, however, there is no reason not to use botulinum toxin injections as the initial treatment of achalasia. If a course of two or three injections seems to be ineffective or is followed by repeated relapses, pneumatic dilatation or, in some cases, myotomy is

indicated. Routine long term treatment with repeated injections should await more data on efficacy and safety.

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