

# Achalasia: Treatment options revisited

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**WA Hoogerwerf, PJ Pasricha. Achalasia: Treatment options revisited. Can J Gastroenterol 2000;14(5):406-409.** The aim of all current forms of treatment of achalasia is to enable the patient to eat without disabling symptoms such as dysphagia, regurgitation, coughing or choking. Historically, this has been accomplished by mechanical disruption of the lower esophageal sphincter fibres, either by means of pneumatic dilation (PD) or by open surgical myotomy. The addition of laparoscopic myotomy and botulinum toxin (BTX) injection to the therapeutic armamentarium has triggered a recent series of reviews to determine the optimal therapeutic approach. Both PD and BTX have excellent short term (less than three months) efficacy in the majority of patients. New data have been published that suggest that PD and BTX (with repeat injections) can potentially obtain long term efficacy. PD is still considered the first-line treatment by most physicians; its main disadvantage is risk of perforation. BTX injection is evolving as an excellent, safe option for patients who are considered high risk for more invasive procedures. Laparoscopic myotomy with combined antireflux surgery is an increasingly attractive option in younger patients with achalasia, but long term follow-up studies are required to establish its efficacy and the potential for reflux-related sequelae.

**Key Words:** Achalasia; Botulinum toxin; Pneumatic dilation

## Achalasie : revue des différents traitements possibles

**RÉSUMÉ :** Les différentes formes de traitement de l'achalasia ont toutes pour but de permettre aux patients de manger sans éprouver de symptômes invalidants comme la dysphagie, les régurgitations, la toux et la suffocation. Pour ce faire, on procédait, autrefois, à la rupture mécanique des fibres du sphincter inférieur de l'œsophage, soit par dilatation pneumatique (DP), soit par myotomie chirurgicale à ciel ouvert. Se sont ajoutées à ces deux méthodes la myotomie par laparoscopie et l'injection de toxine botulinique (TB), ce qui a suscité une série d'examen récents visant à déterminer le meilleur traitement possible. La DP et la TB donnent d'excellents résultats à court terme (moins de trois mois) dans la plupart des cas. Selon de nouvelles données, la DP et les injections répétées de TB pourraient s'avérer efficaces à long terme. La DP est toujours considérée comme le traitement de première intention par la grande majorité des médecins, mais elle comporte un risque de perforation. Quant aux injections de TB, elles se présentent de plus en plus comme une solution valable, sûre, pour les patients jugés mauvais candidats à un traitement plus effractif. La myotomie par laparoscopie, associée à une intervention chirurgicale antireflux, gagne du terrain, surtout chez les jeunes patients, mais il est nécessaire de mener des études de suivi à long terme pour déterminer l'efficacité du traitement et le risque de séquelles possibles liées au reflux.

Achalasia was one of the first gastrointestinal motility disorders to be characterized, both clinically and manometrically. Failure of relaxation of the lower esophageal sphincter (LES) is the cardinal feature of this disease, thought to result from a relatively selective degeneration of the inhibitory neurons in the surrounding myenteric plexus (Figure 1) (1-3). This leads to a functional obstruction of the esophagus that, along with aperistalsis in the body of the esophagus, is responsible for the major symptoms of achalasia: dysphagia for solids and liquids, regurgitation of undigested

food and chest pain. All current methods of treatment are essentially palliative in nature and are focused on reducing the LES pressure. The main focus of this review will be on the use of botulinum toxin (BTX) for this condition and how it compares with other available therapies.

### BTX

BTX blocks the calcium-dependent release of acetylcholine from presynaptic cholinergic nerve terminals. It is a neurotoxin produced by *Clostridium botulinum*. Although several

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*Received for publication May 10, 1999. Accepted May 14, 1999*

serotypes are known, the one used clinically is BTX type A. Pasricha et al (4) were the first to demonstrate the application of BTX for the treatment of achalasia in a double-blind, randomized, placebo controlled study. Since then, multiple studies and several reviews have been published (4-23). BTX causes a significant reduction in resting baseline LES pressure, esophageal clearance and symptoms (Figure 2). The efficacy ranges from 65% to 90% after a single injection, with the effect lasting anywhere from three months to more than one year. The main limitation to the use of BTX for achalasia is its lack of significant long term results with a single injection. With repeat injections at an average of every 10 months, Annese et al (20) recently reported the highest long term efficacy rate to date (75% after a mean follow-up of 24±15 months).

Approximately 80 to 100 U of BTX are injected endoscopically into the LES in four aliquots of 1.0 mL in each quadrant. Preliminary reports have thus far not shown a significant difference in efficacy with higher doses of BTX (17,18); more precise localization of the LES with the use of endoscopic ultrasound or injections over a wider area of the LES are similarly unproven in their effects on efficacy (20,21).

Injection of BTX appears to be safe. The most commonly reported complications are periprocedural transient chest pain and heartburn. Esophageal wall injury and parasophageal tissue inflammation have been reported in two patients (22). Caution needs to be exercised with regard to potential, yet unknown, late side effects. Antibodies may develop against the toxin, causing resistance.

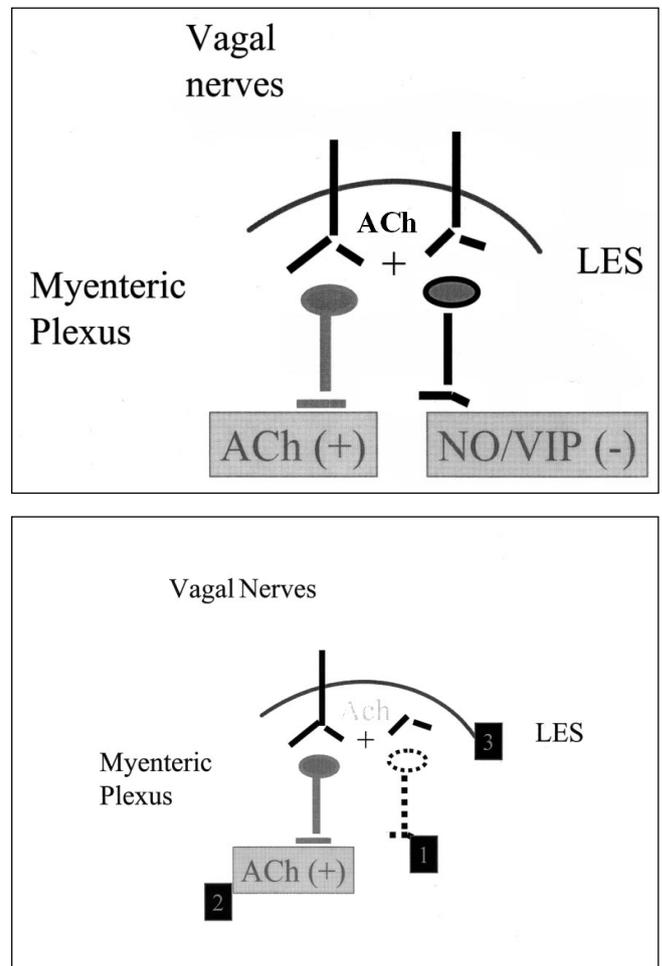
Given its low risk procedural profile, BTX injection is an attractive therapeutic option for high risk surgical patients and elderly patients, in whom conservative, albeit temporizing, management is preferred.

### DRUG THERAPY

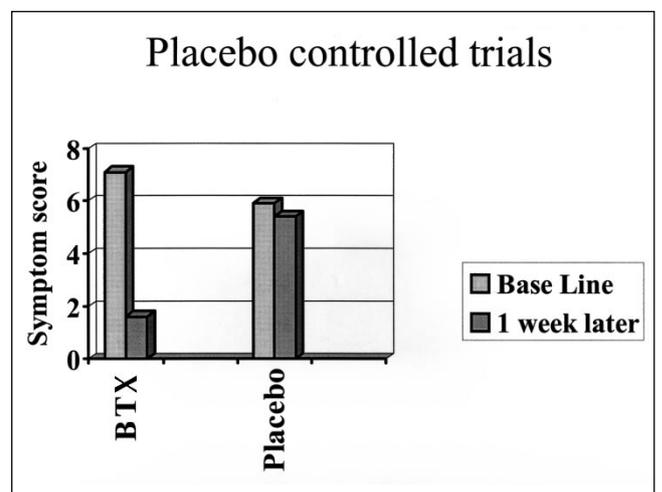
Nitrates and calcium channel antagonists have been recommended for treatment of achalasia. The rationale behind the use of these medications is their potential to decrease LES tone by relaxing gastrointestinal smooth muscle. However, the limitations in the use of these drugs are several: they are short acting; they can have significant side effects such as headaches, hypotension and tachyphylaxis; and, although a decrease in LES pressure has been well documented by manometry, symptom improvement has varied greatly among different studies (24,25). In general, most patients tend to opt for other, more satisfactory forms of treatment after they have been on these drugs for a few months.

### PNEUMATIC BALLOON DILATION

Pneumatic balloon dilation has traditionally been considered the standard, first-line treatment for achalasia. Although the tools for dilation have become more sophisticated (Sir Thomas Willis treated his patient in 1672 by using a whale bone), the principle of therapy has changed little over the centuries. Multiple studies have been published on pneumatic dilation (PD) for achalasia, using different dilators (the older Mosher bag, Sippy dilators, Brown-McHardy, Rider-



**Figure 1) Lower esophageal sphincter (LES) regulation.** **Top** Normal LES pressure can be viewed as a balance between the contractile effects of acetylcholine (ACh) and the relaxing effects of the neurotransmitters nitric oxide (NO) and vasoactive intestinal peptide (VIP) in the myenteric plexus. **Bottom** In achalasia, there is a selective loss of nitrergic neurons in the myenteric plexus (1). This leads to an unopposed excitation of the LES by ACh (2), resulting in a hypertonic LES that fails to relax upon swallowing (3)



**Figure 2) Symptomatic improvement after botulinum toxin (BTX) injection.** There is a statistically significant improvement in symptom score one week after BTX injection as compared to placebo. Data from reference 5

**TABLE 1**  
**Summary of abstracts comparing pneumatic dilation (PD)**  
**with botulinum toxin (BTX) injections**

Author	Number of patients (PD versus BTX)	Initial treatment failure (PD versus BTX)	Efficacy (one month)	Efficacy (one year)
Schroeder et al (15)	9 versus 11	= ( $\pm 35\%$ )	=	
Bansal et al (16)	9 versus 12	= ( $\pm 13\%$ )		=
Vaezi et al (19)	20 versus 22	=		PD > BTX

Moeller dilators, and the now commonly used Rigidflex balloon) and techniques, varying with regard to balloon distention times, balloon pressure, balloon diameter, and rate and number of inflations. A review of the literature by Vaezi and Richter (6) concluded that about two-thirds of the patients have good to excellent symptom improvement after one or more dilations over a mean time of 4.6 years for the older dilators and 1.0 year for the newer dilators. The major drawback of this procedure is the low but significant risk of esophageal perforation, averaging about 5%.

Interpretation of the results of PD is limited by the lack of good prospective studies. Data from one of the few studies of this kind give five-year remission rates of only about 26% from a single dilation, with most patients requiring two or more dilations over a five-year period (26). Retrospective analyses portray a more optimistic outcome, however, with remission rates averaging around 70% or higher (27).

### SURGICAL MYOTOMY

Surgery has been considered the most permanent form of treatment for achalasia. Significant disadvantages include the need for hospitalization and surgical morbidity. The short term efficacy after surgical myotomy is 80% to 90%. However, late relapse, which is felt to occur in part due to longstanding postsurgical gastroesophageal reflux disease, occurs in up to one-third of the patients (28,29). Whether to perform an antireflux procedure at the time of myotomy remains controversial but is generally recommended for abdominal approaches. With the introduction of laparoscopic or thoracoscopic myotomy, surgical intervention has become a more attractive form of therapy (shorter hospital stay and recovery time) (30,31). Short term outcome appears equivalent to open surgical myotomy. However, the long term consequences, especially as related to reflux, are expected to remain problematic.

### COMPARATIVE STUDIES

Despite the abundance of literature on management of achalasia, there appears to be a relative paucity of prospective, randomized controlled studies that directly compare different treatment modalities. Until recently, there have only been two really effective methods of treating patients with achalasia: forceful dilation and surgery. Data from uncon-

trolled retrospective trials have, in general, suggested that success rates were higher after surgery. In a prospective, randomized, controlled trial comparing PD (using a Mosher bag) with surgical anterior esophagomyotomy, Csendes et al (32) demonstrated a five-year response rate of 65% versus 95% in clear favour of surgery.

The common limitation of PD and BTX injection is the lack of long term efficacy, with the need for repeat intervention. The literature has tried to compare the efficacy of one technique with the other. The definition of long term and short term efficacy appears arbitrary because it varies between authors. While some will define one-year follow-up data as short term, others will define a similar time span as long term. Annese et al (8) were the first to publish a randomized, controlled, double-blind study comparing BTX with placebo injections and with PD of treatment failures. One or two BTX injections appeared as effective as PD in short term relief of dysphagia. However, 87% (seven of eight) of the patients required a second injection within one year of the first injection (8). Studies published in abstract form comparing BTX with PD in a prospective, randomized manner are summarized in Table 1. Preliminary data from Bansal et al (16) suggested that the 'short term efficacy' (less than 12 months) of PD and BTX injections are equivalent, but initial treatment failure was significantly higher with BTX (six of 12 patients). On the contrary, Vaezi et al (19) found a significantly higher "long term" efficacy (less than 12 months) with PD compared with BTX. Initial treatment failures, however, were similar for both treatment modalities in this study. Although reviews and meta-analyses clearly suggest a longer lasting effect from a single dilation than from a single BTX injection, a recent study by Prakash et al (23) using survival analysis suggested that BTX injections given as needed have an efficacy similar to a single PD within the first two years of injection. In addition, retreatment with BTX injections may delay the need for subsequent injections.

A major problem in comparative studies is the relative rarity of the disease and the difficulty in maintaining long term follow-up in patients over a five- to 10-year period. The Csendes et al (32) trial took about 15 years to complete and is unlikely to be reproduced. The debate should perhaps now be refocused, not only on efficacy of treatment regimens, but on issues of cost effectiveness and quality of life. As an example, it has been estimated that the long term (seven years) cumulative costs of surgery (approximately \$20,000) are nearly two-and-a-half times more than those of PD, even taking into account the perforation rate and need for retreatment (33). A preliminary cost analysis of BTX injection, PD and laparoscopic Heller myotomy with fundoplication using decision analysis found PD to be the 'least costly initial strategy' (34).

### CONCLUSIONS AND RECOMMENDATIONS

It should be clear from this brief review that the final word on treatment of achalasia is far from being written. Despite some recent advances, therapy remains palliative and each method has a significant drawback. Nevertheless, most patients can

expect to gain good to excellent symptomatic relief of their obstructive symptoms and improvement in their quality of life. With the variety of options available, it is now increasingly possible to tailor the treatment to the needs of the patient. Thus, most young patients, desirous of a single permanent treatment, may be offered a laparoscopic myotomy with the caveat that they should be prepared for long term reflux monitoring and treatment. Others may opt for PD with good expectations from one or two dilations in the first five years. Patients fearful of perforation or those felt to be at high risk for more aggressive therapy may be given a choice of BTX injection, with the understanding that repeat injections will be required periodically.

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