Current Management of Achalasia – A Review

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Abstract

Introduction: Achalasia is a rare oesophageal motility disorder characterised by oesophageal aperistalsis and incomplete relaxation on swallowing of the lower oesophageal sphincter. This review aims to identify and critique literature detailing the available management options for these patients and provide an up to date account of current thoughts and controversies in the treatment of achalasia.

Methods: An extensive literature search was performed for articles and reviews published on the management of achalasia, using Ovid MEDLINE, Cochrane library and PubMed search databases.

Results: The management of achalasia is controversial. Simple options such as pharmacological treatments and Botulinum toxin A injections do not provide sufficient relief of symptoms but may serve to treat those not suitable for surgery or dilatation. However, in those who are deemed suitable, the literature suggests that the optimum treatment is laparoscopic transabdominal Heller myotomy which has demonstrated the best long term results with few complications or perforations.

Conclusion: It is not possible to treat the underlying cause of achalasia but only to improve symptoms. Whilst the literature may suggest that the Heller myotomy is the best method to achieve this, it is clear that the outcomes are dependent on surgeon or physician technique and experience. It is important therefore that these patients are treated in a specialist centre with experience with such procedures. Recent advances in surgical and endoscopic technologies, with robotic Heller myotomy and per-oral endoscopic myotomy, provide promising progress for the treatment for achalasia

Keywords: Achalasia, manometry

INTRODUCTION

Achalasia is a rare oesophageal motility disorder, typically presenting with symptoms of dysphagia, regurgitation of food and retrosternal chest pain made worse on eating. The annual incidence in the UK, Ireland and USA is between 0.5 to 1.2 per 100,0001 and seems to affect both sexes and all races equally.

The aetiology of achalasia remains largely unknown. However, suggested influences include a genetic predisposition, infection and autoimmunity2,3. The changes responsible for achalasia include a combination of both poor oesophageal contractility and impairment of relaxation of the lower oesophageal sphincter resulting in oesophageal distension and symptoms described above. Reaching a diagnosis relies on oesophageal manometry in addition to barium swallow and oesophagogastroduodenoscopy (OGD).

The condition was first described by a British physician in 1674, Sir Thomas Willis, and treated with dilatation using a sponge attached to a whale bone4. It was not until many years later in 1913 that a German surgeon, Heller, performed the first cardiomyotomy5. The optimal treatment for achalasia remains controversial with treatment largely dependent on the preference of the physician. Cases are few and far between and therefore large studies reviewing the optimal treatments are limited.

This review aims to identify and collaborate relevant literature detailing the management options available to treat achalasia.

METHODS

An extensive literature search was performed using Ovid MEDLINE, Cochrane library and PubMed databases for relevant articles relating to medical, endoscopic and surgical management of patients with achalasia. Keywords including achalasia, Heller’s myotomy and balloon dilatation were used and relevant articles included.

MANAGEMENT

Diagnosis

All patients presenting with dysphagia should initially be investigated with OGD to exclude a mitotic lesion. OGD has little value however in diagnosing achalasia but remains an essential component of the investigation of the upper gastrointestinal tract. The gold standard for diagnosing achalasia is oesophageal manometry6,7. This typically shows a high resting pressure in the lower oesophageal sphincter which fails to relax on swallowing with associated impaired oesophageal contractility. A barium swallow may show very little in early disease, but in more advanced disease may demonstrate a ‘bird’s beak’ appearance or a sigmoid oesophagus, distension due to longstanding obstruction at the gastro-oesophageal junction (GOJ)8.

Achalasia Subtypes

Whilst the diagnosis of achalasia is dependent upon the above, high resolution manometry can further classify achalasia into
three subtypes dependent on the pattern of oesophageal peristaltic abnormalities and oesophageal pressure dynamics (Figure 1). The three subtypes differ in responsiveness to treatment and as such, can be used to guide the most appropriate treatment and counsel patients appropriately.

Figure 1: The Chicago classification for achalasia subtypes

| Type I (classic) | Achalasia with minimal oesophageal pressurisation |
| Type II         | Achalasia with oesophageal compression |
| Type III        | Achalasia with oesophageal spasm |

**Treatment**

The treatment for achalasia is aimed entirely at symptom control. The underlying pathological processes which lead to myenteric plexus neurodegeneration are not fully understood and as such, cannot as yet be prevented or reversed. Current treatment options exist therefore to reduce the contractility of the lower oesophageal sphincter and hence improve the obstruction to passage of food and symptoms of dysphagia.

Various options exist for this, including pharmacological therapies which are available in the form of nitrates, calcium channel blockers, anticholinergic agents and beta agonists. Endoscopic therapy is a preferable alternative, with pneumatic balloon dilatation or intraspincteric Botulinum toxin injection being the most commonly used techniques. The ultimate and generally accepted optimal treatment, however, is the surgical Heller’s myotomy (Figure 2).

Figure 2: Treatment options available for the management of achalasia

| Pharmacological options | Oral nitrates (GTN, Isosorbide dinitrate) |
|                        | Calcium channel blockers (Nifedipine, verapamil) |
|                        | Anticholinergics |
|                        | Opioids (loperamide) |
|                        | Phosphodiesterase inhibitors |
|                        | β₂ agonists |
|                        | Nitric oxide agonists |
| Endoscopic techniques | Pneumatic balloon dilatation |
|                        | Botulinum toxin injections |
|                        | Percutaneous endoscopic myotomy (POEM) |
| Surgical options       | Heller’s cardiomyotomy (transabdominal or transthoracic / open or laparoscopic) |

**Medical**

Pharmacological therapies as treatment for achalasia have been largely superseded by improvements in both endoscopic and surgical techniques. However, their potential role still exists in those with early disease, in elderly patients unsuitable for surgery or dilatation and in whom Botulinum toxin injections have failed. They may also have potential use in patients awaiting surgery for interim symptom control. Most trials reviewing the effect of drug therapy for achalasia are limited by small numbers and short follow up so long-term benefits remain poorly understood.

As with all achalasia treatments, the aim of drug therapy is to relax the lower oesophageal sphincter. Nitrates have been used as vasodilators within cardiovascular disease since the 1970s. Within the smooth muscle of the gastrointestinal tract, they behave similarly by increasing the production of cyclic GMP and in turn, causing dephosphorylation of the myosin light chain and subsequent inhibition of smooth muscle contraction. It is with this concept in mind that medical treatment with nitrates can cause relaxation of the lower oesophageal sphincter. There are only two randomised controlled trials which have reviewed the effect of nitrates on patients with achalasia and compared them to alternative treatment modalities. However, as a Cochrane review has established, the results of these studies cannot be reliably interpreted due to both the methodology and the limitations with regards to follow up. Regardless, nitrates are not without side effects and can cause headaches and changes in blood pressure. In view of this, their routine use is not recommended.

Calcium channel blockers, including Nifedipine, are more commonly used and are given sublingual 15-30 minutes before meals. These limit the intracellular uptake of calcium and hence reduce the contractility of muscle cells. Reports of success as high as 65-80% have been documented. However, up to 30% experience significant side effects.

Additional agents that have been described include β₂ agonists, anticholinergics and phosphodiesterase inhibitors, the latter of which induces nitric oxide release and thereby relaxation of lower oesophageal sphincter muscle but can also result in significant side effects, including angina, and so routine use is again not advised. It is for these reasons, that progress has been encouraged elsewhere with developments in both endoscopic and surgical techniques for the treatment of achalasia.

**Endoscopic**

Endoscopic treatments are again aimed at reducing the contractility of the lower oesophageal sphincter and several options exist for this. Injection of Botulinum toxin A is the most commonly performed and has fewer associated side effects and complications than its alternatives, hence is often used as first line treatment and especially in patients not suitable for surgical intervention. Alternative options include pneumatic balloon dilatation and more recently, per-oral endoscopic myotomy (POEM).
Botulinum toxin A is used as an intrasphincteric injection and exerts its action by inhibiting the release of acetylcholine, necessary for muscular contractions. This in turn lowers the tone and pressure of the lower oesophageal sphincter. 80-100 units of Botulinum toxin A are injected in divided doses in all four quadrants at the level of the squamocolumnar junction via endoscopic guidance. Patients recover quickly and can go home the same day\textsuperscript{22}, typically seeing improvements in symptoms between days 1-3\textsuperscript{22}. Results are variable. Certainly the side effects are minimal and it appears to be a safe procedure without the risk of perforation seen with other techniques\textsuperscript{24,25}. Short term improvement in symptoms is described as high as 85%. However, over time this is seen to decrease significantly to only 30% at one year. Most will require further injections or alternative treatments such as pneumatic balloon dilatation or surgical myotomy\textsuperscript{24}.

Pneumatic balloon dilatation includes inflating a 30mm balloon at the level of the GOJ\textsuperscript{26,27}. This process fractures the muscular fibers of the lower oesophageal sphincter hence disrupting the sphincter mechanism. It can be performed under fluoroscopic or endoscopic guidance dependent on operator experience and preference. The major risk is oesophageal perforation, which in experienced hands occurs in 1.9% (range 1-16)\textsuperscript{28}. In addition, gastro-oesophageal reflux post procedure can be troublesome, affecting 4-16% of patients\textsuperscript{29,30}.

A Cochrane review compared outcomes with Botulinum toxin injections and pneumatic balloon dilatation\textsuperscript{31}. Whilst little difference in short term improvement was noted, longer term remission rates were considerably higher in those treated with balloon dilatation. However, even with balloon dilatation, up to a quarter require further treatments at five years\textsuperscript{31,32}.

An emerging endoscopic technique is the peroral endoscopic myotomy (POEM). This is performed by incising the mucosa endoscopically, dissecting and developing a plane in the submucosal layer and performing a myotomy inferiorly to beneath the gastro-oesophageal junction. The mucosa is thereafter closed with staples. Studies have shown it to be both safe and effective with short term results demonstrating similar relief in dysphagia and improvements in Eckardt scores as patients undergoing laparoscopic myotomy\textsuperscript{33,34}. The added benefit of POEM is the potential for faster return to normal activities\textsuperscript{34} and with preserving the need for surgery, dissection at the hiatus can be avoided which may reduce symptoms of post-operative reflux. However, it is technically challenging and studies demonstrating long term outcomes are not yet available.

**Surgical**

The surgical treatment for achalasia involves performing a myotomy at the level of the gastro-oesophageal junction. There has been controversy regarding the most appropriate method of achieving this and experience includes open versus laparoscopic, transthoracic versus transabdominal. Further controversy exists in the importance of performing simultaneous antireflux surgery.

With the development of laparoscopic abdominal surgical treatments are aimed at disrupting the lower oesophageal sphincter mechanism and none are without risk or complication. Treatment modalities vary in their short and long term success rates. Pharmacological treatments are of limited

Surgical myotomy offers superior long-term relief of achalasia-related symptoms compared to medical and endoscopic alternatives, alleviating dysphagia in 88%-94% at ten years following surgery\textsuperscript{36,37}. Improvements have also been demonstrated in patient satisfaction and quality of life post operatively\textsuperscript{38}. Performing a complete myotomy is essential to outcome and prevention of recurrent symptoms, hence accuracy and precision is paramount\textsuperscript{39}. Where this is concerned, robotic surgery is becoming more accessible and early results would suggest improvements over conventional laparoscopic surgery\textsuperscript{40}.

The risk of perforation is small with laparoscopic myotomy\textsuperscript{41} and even smaller with robotic surgery. The main complication associated with performing a myotomy is symptomatic reflux. Controversy exists regarding simultaneous anti-reflux procedure and some would argue that in the absence of posterior dissection at the level of the GOJ, there is not the need\textsuperscript{42}. A meta-analysis performed by Lyass et al reviewed patients undergoing surgery for achalasia\textsuperscript{43}. The authors concluded that the rates of reflux post operatively were no different between those who had anti-reflux procedures and those who did not. Ultimately, the decision to proceed with anti-reflux surgery will vary surgeon to surgeon. However, what is generally accepted is that a complete 360 degree Nissen’s fundoplication is not required, and may serve only to give the patient ongoing symptoms of dysphagia. Therefore, Toupet (posterior 270 degrees) or Dor (anterior 180 degrees) fundoplication are more commonly used, the latter providing cover to the myotomy and thus potentially protecting any unidentified mucosal breach\textsuperscript{44}.

**Surveillance**

Studies have demonstrated that patients with a diagnosis of achalasia have an increased risk of squamous cell carcinoma of the oesophagus\textsuperscript{45}. For this reason, guidelines developed by the American Society for Gastrointestinal Endoscopy suggest surveillance oesophagogastroduodenoscopy every 1-3 years for 15-20 years\textsuperscript{46}.
value and Botulinum toxin injections have limited long term results but both may play a role in patients who cannot tolerate more invasive procedures\textsuperscript{18}. The main debate has historically lain between advocating the use of endoscopic dilatation versus laparoscopic Heller myotomy.

Studies looking at endoscopic dilatation versus myotomy have comparable initial symptomatic relief. Direct comparison between the long term outcomes does, however, favour laparoscopic myotomy\textsuperscript{20,50}. Traditionally, endoscopic dilatation has been the first line treatment, with surgery reserved for those in whom dilatation has failed\textsuperscript{51}. However, subsequent intervention is common and there are many studies examining outcomes of second treatment with either surgery or dilatation. In cases where initial treatment has failed and recurrent symptoms of dysphagia present, dilatation has been shown to be more effective in those who have had surgery rather than those who have had previous dilatations or Botulinum toxin injections\textsuperscript{22-53}. Importantly, there is not a greater risk of perforation in these patients than in those who have not undergone myotomy\textsuperscript{34}.

Performing a surgical myotomy after previous treatment with dilatation or injection may complicate the surgery slightly and has been shown to increase complications and failure of myotomy\textsuperscript{55,56}, providing an argument for surgery as first line treatment. That said, surgery is still recommended in these patients as the most successful option\textsuperscript{57}.

Ultimately, the optimal treatment will vary dependent on physician or surgeon technique and experience. Cases are limited and so it is recommended that these patients are treated in a specialist Upper GI unit where all options are presented to the patient and the risks and benefits of each counselled appropriately. It is an exciting time for achalasia as new treatment options including POEM come to light and robotic surgery becomes more available.

Competing Interests
None declared

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