Sedation outside the operation room

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ACHALASIA AND PERORAL ENDOSCOPIC MYOTOMY POEM

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Chapter 4

SUMMARY

Achalasia describes a clinical picture where the motility of the oesophagus is malfunctioning and the relaxation of the lower oesophageal sphincter (LOS) during swallowing is inadequate. The reasons of achalasia are not clarified yet. Achalasia results in a stasis of food and liquids with a wide range of other symptoms. There are various treatment options. Medication is rarely successful. Balloon dilatation and surgical myotomy of the LOS can reduce symptoms in 60-90% of patients. For the last few years, myotomy has been made possible by means of peroral endoscopic myotomy (POEM). POEM is performed under general anaesthesia at the endoscopy suite. Key points from an anaesthesiologic point of view are an increased risk of aspiration and procedure specific complications, including perforation, pneumomediastinum, pneumoperitoneum, and pneumothorax.
INTRODUCTION

Achalasia is a rare and disabling disease that is characterised by reduced motility of the oesophagus, coupled with the inability of the lower oesophagus sphincter (LOS) to relax sufficiently. The word achalasia is derived from the Greek word (a)chalasis, which can be translated as "no relaxation". Patients usually experience retrosternal pain and progressive dysphagia, when taking solid or liquid food. The basic causes of achalasia are not known yet. In this article, we will discuss the clinical picture of achalasia and the possible treatment options. Moreover, we will focus on a relatively new endoscopic treatment for achalasia: the peroral endoscopic myotomy (POEM). At the moment, this technique is being used only in two hospitals in the Netherlands and is performed under general anaesthesia outside the operation room at the endoscopy suite.

EPIDEMIOLOGY

Achalasia is an uncommon disease. Worldwide, the incidence is approximately 1 of 100,000; this means in the Netherlands, there are approximately 1500 patients. This disease has a significant impact on the quality of life, efficiency of labour, and functional status of the patient. An additional problem is that patients often have to undergo several invasive interventions.

PATHOPHYSIOLOGY

The pathophysiology of achalasia is largely unknown. An association with the Down syndrome and Parkinson’s disease, familial accumulation, and the results of twin studies suggest a partial genetic basis for this disease. In addition, viral infections and immunologic factors could also become important; it seems that autoimmune diseases are more common in patients with achalasia. T-lymphocytes have an important role in this context. Achalasia is on histopathological examination characterised by the destruction of ganglion cells in the plexus myentericus of the distal oesophagus and the LOS. The plexus myentericus is important in the coordination of oesophageal peristalsis. In patients with achalasia, this plexus is infiltrated by T-lymphocytes. This results in a reduced activity of inhibitory neurons and an imbalance between activation and relaxation of the smooth muscle fibres of the oesophagus and LOS. The result of this imbalance is an impaired relaxation and excessive contractility of the muscle layer leading to constriction of the oesophageal lumen with shortening during swallowing and an abnormal peristalsis with an increased tonus in the LOS. The outcome of this combination is stasis of food, liquid, and saliva above the LOS.
DIAGNOSTIC

The typical symptoms of patients with achalasia are dysphagia, retrosternal pain, and pyrosis (Table 1). On average two years after symptoms from oesophageal dysphagia, 40% of these patients develop respiratory complaints due to (micro) aspiration.\textsuperscript{1,2}

If a patient shows symptoms that may fit to achalasia, it is important to exclude more common disorders like gastro-oesophageal reflux, mechanical obstruction by malignancy of the oesophagus or surrounding tissues, strictures, foreign bodies, eosinophilic oesophagitis, or systemic neuromuscular diseases.

The key test for establishing the diagnosis achalasia is oesophageal manometry. During manometry a thin probe with pressure sensors is inserted through the nose and placed in the oesophagus while the patient is asked to swallow several times. Results are graphically displayed on a "map" which indicates the pressure in different locations at different points in time (Figure 1). In addition to the manometry, barium swallow is performed. Patients have to swallow barium contrast solution at different times (usually after 0, 1, 2, and 5 minutes).

In achalasia, normal oesophageal motility is absent. The oesophagus above the narrowing of the LOS is often dilated showing a typical "bird's beak"- or corkscrew pattern (Figure 2). The same signs can be observed during oesophago-gastroscopy: oesophageal dilatation, abnormal ‘twists’, and stasis of food. It could be difficult or impossible to pass the gastro-oesophageal junction due to hypertonia of the LOS. Another typical finding is a pattern of candidiasis as a result of stasis of food.

On the basis of manometry results, achalasia can be divided into three subtypes (Figure 3). Type I indicates an impaired relaxation of the LOS with lack of peristalsis, but with a normal oesophageal pressure. Type II is characterised by an increased oesophageal pressure. In type III, additionally spastic contractions of the distal oesophagus are observed. Achalasia Type II has the best prognosis after treatment, while type III has the worst.\textsuperscript{1}

Table 1. Symptoms of achalasia

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>% of patients</th>
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<tbody>
<tr>
<td>Dysphagia</td>
<td>90%</td>
</tr>
<tr>
<td>Pyrosis</td>
<td>75%</td>
</tr>
<tr>
<td>Regurgitation or vomiting</td>
<td>45%</td>
</tr>
<tr>
<td>Retrosternal pain</td>
<td>20%</td>
</tr>
<tr>
<td>Upper abdominal pain</td>
<td>15%</td>
</tr>
<tr>
<td>Pain during swallowing</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Cough</td>
<td>20-40%</td>
</tr>
<tr>
<td>Chronic aspiration</td>
<td>20-30%</td>
</tr>
<tr>
<td>Hoarseness or sore throat</td>
<td>33%</td>
</tr>
<tr>
<td>Unwanted weight loss</td>
<td>10%</td>
</tr>
</tbody>
</table>
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Figure 1. Manometry of a healthy person (left) and patient with achalasia type I (right)

Figure 2. Barium swallow with a typical "bird's beak"- or corkscrew pattern in a patient with achalasia

THERAPY

Causal treatment of achalasia is not possible. Altogether, there are four treatment options: medication, injection of botulinum toxin into the LOS, pneumatic dilatation of the LOS, and (surgical) myotomy.

Medication

Drugs that can reduce the pressure in the LOS are calcium channel blockers, nitrates, and phosphodiesterase inhibitors. Evidence based data is missing, but treatment with these agents is rarely successful and therefore not usually performed.
Figure 3. Subtypes of achalasia differentiated by manometry and barium swallow
Type I indicates an impaired relaxation of the LOS with lack of peristalsis, but with a normal oesophageal pressure. Type II is characterised by an increased oesophageal pressure. In type III, additionally spastic contractions of the distal oesophagus are observed.

Injection with botulinum toxin
Botulinum toxin blocks the release of acetylcholine in neurons. The injection can be performed endoscopically under mild sedation. It leads to a reduction of symptoms in two-thirds of the patients with achalasia. Unfortunately, a drawback is that the effect is only temporary due to the regeneration of neurons and patients typically need to be re-treated within a year. Alongside, it is a problem that repeated injections with botulinum toxin complicate Heller myotomy, one of the more definitive treatment options.\(^1\)

Pneumatic dilatation
A rigid balloon is placed in the LOS and filled with air (Figure 4). The procedure is performed under deep sedation. 60-90% of the patients benefit from the dilatation, but approximately one-third of these patients need to be retreated after a few years. A recent randomised study showed that repeated pneumatic dilatations are comparable with surgical myotomy.\(^1,3\)

The most important complication is perforation of the LOS. The incidence of perforation is about 1%.\(^1\)
Surgical myotomy

During laparoscopic Heller myotomy the outside muscle layers of the LOS are cut. Heller myotomy is performed under general anaesthesia. Success rate is around 90%. The most important complication is perforation of the stomach. The risk of perforation is the same in Heller myotomy as in pneumatic dilatation. In order to prevent gastro-oesophageal reflux, myotomy is combined with a fundoplication (Figure 5). Nowadays, myotomy can also be performed endoscopically: peroral endoscopic myotomy (POEM). This treatment is discussed below.

PERORAL ENDOSCOPIC MYOTOMY (POEM)

The first POEM was performed 2008. POEM is performed under general anaesthesia. A mucosal incision in the middle segment of the oesophagus is made and the submucosal layer of the oesophagus and the cardia of the stomach endoscopically transformed into a tunnel through which oesophageal myotomy is carried out. During the procedure, the
oesophagus and submucosal tunnel are inflated with carbon dioxide. The right level of the tunnel is found by direct visualisation and injection of liquid, e.g. methylene blue. The right direction is determined by direct visualisation of the circular muscle layers. Among patients in a late stage of disease, the orientation can be complicated by fibrosis of the surrounding tissue. It is important that the fibres are cut over by the entire thickness of the circular muscle layer. At the end, the mucosa opening is closed with clips (Figure 6).

Before performing a POEM, active candidiasis should be treated. The most formidable - but fortunately rare - complications of POEM are perforation, bleeding, and infection. Concerning bleeding, it is necessary to treat submucosal tissue carefully to avoid the risk of bleeding from submucosal vessels or mucosal laceration. Minor bleedings can be tamponed or coagulated by electrocoagulation. In major bleedings the use of a Blakemore-Sengstaken tube - a flexible catheter with oesophageal and gastric balloon - that can apply pressure on the surrounding tissue when inflated has been sporadically reported. However, there are also studies that discourage the use of this tube since there is a smaller barrier after myotomy that can prevent bleeding into the mediastinum or peritoneum. In a more advanced stage of achalasia, bleeding can occur more easily due to neovascularisation. Perforation can result in tension pneumothorax, pneumomediastinum, pneumoperitoneum, and subcutaneous or submucosal emphysema. These complications should be treated according to current guidelines by the anaesthesiologist or endoscopist. Prospective studies were able to show that POEM is successful in more than 90% of the patients. This also applies to patients with type III achalasia.

Perioperative care

Perioperatively, it is important - independent of the treatment form - to take measures to prevent aspiration. It is also important to be aware of a (small) risk of perforation during and after pneumatic dilatation, the Heller myotomy, and also POEM. Heller myotomy is performed laparoscopically with all risks of this operative procedure. POEM can additionally be complicated by pneumomediastinum, pneumoperitoneum, and submucosal or subcutaneous emphysema aggravated by carbon dioxide insufflation. This can cause extremely high airway pressures even with low tidal volumes and hypercapnia. Treatment is to vent pneumoperitoneum by using an ultrasound guided 14-gauge infusion needle placed into the pneumoperitoneum. In case of developing subcutaneous emphysema around neck and face, it is recommended to assess the possibility of re-intubation before extubation of the trachea by direct laryngoscopy. Optionally, extubation should be delayed until reduction of the emphysema. The available literature on perioperative care of patients with achalasia is unfortunately very limited. There are no controlled studies or approved guidelines concerning preprocedural fasting, airway management, and other anaesthesia techniques.
Figure 6. POEM (picture by courtesy of Ron Slagter)
(a) Mucosal incision (b) Submucosal tunnel (c) Myotomy (d) Closure
Studies

Three retrospective cohort studies with specific focus on anaesthesia technique during POEM have recently been published.\textsuperscript{5,7,8}

In 2014 Tanaka et al.\textsuperscript{7} reported on 28 patients who underwent POEM after 24 hours fasting. Before POEM, these patients underwent oesophago-gastroscopy under sedation with the aim to remove remaining food in the oesophagus and stomach. Afterwards, their trachea was intubated after administration of propofol, remifentanil, and rocuronium (a specific method of intubation was not described), and anaesthesia was maintained with sevoflurane and remifentanil. During the following endoscopy, it was noticed that still in ten patients solid food and in four patients liquid was in the oesophagus. One patient developed subcutaneous emphysema. No other complications were observed. All patients could easily be extubated.\textsuperscript{7}

In 2015, Yang et al.\textsuperscript{8} described 52 patients who underwent POEM in the US. All patients had nothing per os for eight hours and had fed for a varying period from 48 hours up to 5 days only upon clear liquids. All patients received preoperative antibiotics and proton pump inhibitors until discharge home. Intubation was performed as “rapid sequence induction” (RSI) (medication is not reported) and anaesthesia was obtained with propofol and/or sevoflurane. No regurgitation or aspiration was observed during induction. Postoperatively, all patients had a chest x-ray and on the day after procedure barium swallow or a CT scan with oral contrast to eliminate leakage. Patients received a soft pureed diet for two weeks. Some patients developed high ventilation pressures during procedure that could be easily remedied by endoscopic decompression of the stomach. Six patients had a pneumoperitoneum, for which decompression of the abdomen with a Veres needle was necessary. Except for one patient with severe COPD, all patients could be extubated in the endoscopy room. Four patients experienced perforation of the oesophagus. In three patients this was noticed and treated immediately during procedure. Perforation in the fourth patient was discovered on the day after procedure during barium swallow. This patient had to undergo laparoscopic repair combined with temporary placement of an endoluminal stent. All patients fully recovered. There were no bleeding complications. Two patients developed pneumonia after the procedure. The average length of stay in hospital was 3.5 days (range 2-10 days).

Several months ago, a third case series of 24 patients was published.\textsuperscript{5} Again, there was neither uniform fasting policy nor airway management. Fasting time varied from 6 up to 25 hours. Sixteen patients received standard induction without special measures to prevent aspiration, 7 patients received RSI with cricoid pressure and one without. One
patient experienced an aspiration after a standard induction. Procedure was cut short and recapped on a later moment when the patient was successfully intubated after a rapid sequence induction with cricoid pressure. Anaesthesia was maintained with sevoflurane, desflurane or propofol. In contrast to our own experiences, the authors stated that POEM is relatively painless requiring only small amounts of opioids.\(^8\) Regarding airway management, Saxena et al.\(^9\) suggest in a reply letter to Tanaka et al.\(^7\) the use of a special tube with the possibility of suction of irrigation fluid under the glottis and above the cuff (TaperGuard Evac, Covidien). The authors intubated 35 patients who underwent POEM with this special tube and experienced no aspiration.\(^9\) However, this also can be achieved by using the suction canal of the endoscope during withdrawal from the oesophagus.

**Own experiences**

Nearly 160 POEM procedures have been performed in the AMC. All patients scheduled for POEM have to follow a strict liquid diet for three days prior to the procedure. Twenty-four hours before procedure they may only take clear liquid and 8 hours before nothing more by mouth. During time out, patients will be asked about their own feeling of stasis of food in the oesophagus. All patients are intubated in a RSI setting without cricoid pressure. In doubt of stasis in the oesophagus, awake fiberoptic intubation with remaining airway reflexes is the option of choice. Until now, we did not have any aspiration during intubation. Alternatively, it is an option to start with an oesophago-gastroscopy under light sedation to remove remaining food in the oesophagus and stomach. We have not yet applied this method. There is no specific protocol for medication during induction or for maintenance of anaesthesia. Our data show that POEM is a painful procedure. Therefore, all patients receive multimodal intravenous pain therapy with acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs) or alternatively metamizol, esketamine, and an opioid combined with co-analgesics like clonidine and dexamethasone.

The first hours after procedure, patients stay in the recovery room and are titrated with morphine as necessary. Usually, intravenous treatment with paracetamol, NSAID, or metamizol is sufficient. The first 24 hours patients are not allowed to eat and drink, so they are treated with a crystalloid and glucose infusion for this time. After the barium swallow on the first postprocedural day, patients start with clear liquid followed by liquid diet that is slowly extended. Patients are treated with omeprazole for two weeks after the procedure. For most patients pain medication is still necessary in the first two to three days postoperatively.
**Conclusion**

In the absence of controlled studies in patients with achalasia and a limited anaesthesiologic experience of POEM, it is not possible to make strong recommendations. The methods as described above seem to provide an effective and safe treatment option. We strongly recommend a strict fasting protocol in patients with achalasia and measures to prevent aspiration, such as RSI. The preprocedural ‘cleaning’ oesophago-gastroscopy seems not to be necessary and is probably very uncomfortable for the patient.
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REFERENCES