Treatment of Achalasia

Dr. Javad Mikaeli
Professor of medicine
Digestive Disease Research Center
Tehran University of medical sciences
Treatment of Achalasia

- There is no cure for the disease

- Treatment is focused on palliating symptoms by decreasing LES pressure:
  - 1- Mechanical disruption of the muscle fibers of the LES
  - 2- Biochemical reduction in LES pressure
Treatment options for Achalasia

- Medical therapy
- Pneumatic dilatation
- Cardiomyotomy
- Botulinum toxin injection
- Ethanolamine injection
- Combined methods
Early recognition of achalasia offers the best chances for an adequate treatment and prevention of complications such as weight loss and dilation of the esophagus.

Severe esophageal dilation significantly reduced the response to treatment (OR 0.2 compared with no dilation).
Images in clinical medicine
Achalasia

Smooth-Muscle Relaxants

- The drugs are taken sublingually 10 to 30 minutes before meals.

- **Side effects** are headache and hypotension for nitrates and peripheral edema for calcium channel blockers.
Achalasia
Smooth- Muscle Relaxants

- The efficacy of nifedipine ranged from 50 to 90%, with side effects seen in up to 30% of patients.

- Pharmacotherapy is frequently associated with tachyphylaxis.
BOTULINUM TOXIN

**BTX** reduce the LES pressure by selectively blocking the release of acetylcholine from cholinergic nerves in the myenteric plexus.
Botulinum Toxin Injection

- A response to BT supports the diagnosis of achalasia if the diagnosis is uncertain based upon manometry.

- Improvement in symptoms is usually observed after 24 hours; peak effects occur later in some patients.
Achalasia  
Botulinum Toxin Injection

- **The overall efficacy**: 65 to 90% after one injection

- **Relapse rates**: >50% within 6 to 12 months

- **Symptom relief**: 75% with repeat injections during 2 years follow-up
Achalasia
Botulinum Toxin Injection

- **Indications:**
  - Sigmoid esophagus
  - Severely malnourished patients
  - Advanced cardiopulmonary diseases
  - Epiphrenic diverticula
  - Patient’s will
ACHALASIA (BT)
Predictors of good response

- Age > 50 years
- Vigorous achalasia (type 2)
- The 100 X 2 IU botox regimen at four weeks interval

Annese has reported remission rate of 68% at 2 years with this regimen.
INFLUENCE OF ACHALASIA SUBTYPES

- Compared with type I patients, type II patients were much more likely to respond to any kind of therapy (OR 11.2), whereas patients with type III were much less likely to respond to any therapy (OR 0.24).

- **Myotomy** may only be advantageous in type I patients.
Botulinum Toxin Injection

- **Complications**:
  - Transient chest pain (25%)
  - Transient heartburn (5%)
  - GERD (<5%)

- Antibodies to BT have been detected in patients who were secondary treatment failures.
Surgery after BT or PD

- Would prior BT or PD cause some degree of difficulty during surgery?

- As a better explanation, there may be a subset of patients that is refractory to all forms of treatment, including myotomy.
PD versus BT injection

- Five trials compared PD with BT in patients followed for at least 12 months.

- PD was associated with a significantly higher remission rate.
- Lower relapse rate.
- Longer time to relapse.
RCT comparing BT to PD

- The 1 year remission rate:
  - Single PD (53%)
  - Single BT (15%) \((P<0.01)\)
  - Redilation (100%)
  - Reinjection (60%) \((P<0.01)\)
Achalasia

PD versus BT

- PD and BT have similar efficacy during short-term follow-up.

- Repeated therapy with BT is necessary to maintain efficacy.
**Achalasia**

**Pneumatic dilation**

- **Good to excellent short-term results**: 60 to 85% with a single PD.

- **Success rates will be declined with time**: (68% at 12 months and 58% after 36 months).

- **Repeated dilations using an "on demand" approach** lead to remission in the majority of patients (> 90% at 10 years).
Achalasia
Graded Pneumatic dilation

- The most popular pneumatic dilator is the Rigiflex balloon. (Boston Scientific Corp, Boston, MA)

- The smallest size balloon (3.0 cm) is typically used for the first session.

- If symptoms persist, the procedure can be repeated with incrementally larger balloons. "graded approach"
**PD - the "progressive" method**

- A series of progressively larger dilations on the same or successive days until "satisfactory" manometric and/or radiographic criteria are met.

- A retrospective study of 209 patients found that **the response** to a single series of dilations was **66 percent at six years.**
DILATION OF THE LOWER ESOPHAGEAL SPHINCTER

- Esophageal dilation with a soft, tapered dilator (bougienage) is usually provides only temporary and incomplete relief of symptoms.

- It is an option in patients who are poor surgical candidates because it has a lower risk of perforation compared with PD.
We evaluate patients within one month after each procedure by symptom score and timed barium esophagogram.

The degrees of patient symptom improvement and the esophageal emptying in esophagogram were not always correlated.
Timed Barium Esophagogram
# Timed Esophagogram

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Achalasia
Pneumatic dilation

- Most relapses and need for a second PD occur in the first 12 months.

- 25 to 50 percent of patients relapsing over a five year period.

- Those who stay well in the first five years or so are likely to continue to do well.
Achalasia
Pneumatic dilation

- PD may not be equally effective for relieving all symptoms.

- In one report, PD had little effect on **chest pain**, which is present in 40 to 60 percent of patients.
Achalasia

Complications of PD

- **Perforation** (2-6%)
- **Bleeding**
- **Intramural hematoma**
- **Diverticula at the gastric cardia**
- **Severe postprocedural chest pain** (15%)
- **GERD** (2%)

- **Mortality** (0.2%)
Pneumatic Dilation

Complications (perforation)

- Usually present in the first dilation session, in the distal left side of the esophagus.

- Findings: tachycardia and chest pain that lasts for more than four hours.

- May be managed with conservative treatment such as antibiotics and parenteral nutrition.
Clinical deterioration or the presence of free-flowing barium into the mediastinum requires immediate thoracotomy and repair.

- Mortality rate can be very high (5-75%) and correlates with delays in both diagnosis and treatment.
Pneumatic Dilation

Complications (perforation)

- The endoscopic closure by clips is indicated when the diagnosis is made during the PD.

- However, observation of worsening signs and a tight cooperation with the thoracic surgeons is recommended.
Pneumatic dilation
predictors of outcome

- Post-dilation LES pressure (<10 mm Hg)
- Older age (>40 years)
- Female sex

Young males may benefit from an initial PD with a 3.5 cm balloon.
Achalasia

Pneumatic dilation

- Other forms of therapy should be considered for patients who have had two or three unsuccessful PDs.

- PD should be attempted before myotomy during pregnancy.
ACHALASIA

Efficacy of BT before PD

- BT before PD would benefit a group of achalasia patients.
- We can use combined treatment in the patients do not respond well to two sessions of PD (especially in older patients $>40$ years old).
- Interval between BT & PD: one month (in our study), 7 days (Hep A study), simultaneous (Chinese study)
ACHALASIA

Efficacy of BT before PD

- In a RCT 90 patients were assigned to BT, PD, or both BT injection and PD.

- The response rate at two years was significantly higher with combination therapy (57% versus 14% with BT and 36% with PD).
Achalasia- Myotomy

- Open surgical myotomy
- Laparoscopic Heller myotomy
- Robotic Heller myotomy
- Peroral endoscopic myotomy
Achalasia - Myotomy

- Response Rate:
  - At 1 year: 85-90%
  - At 10 years: 70-85%
  - At 20 years: 65-73%

- Mortality Rate: 0.03%
  - Mortality rate is similar to PD
Surgical Myotomy

- The addition of a fundoplication reduce the rate of postmyotomy GERD (4 versus 32 percent).
Laparoscopic myotomy

A single-center series of 407 patients

- The five-year response rate was 87 percent.

- **Most failures** occurred **within 12 months**, and the majority of patients were treated with PD.

- The presence of **chest pain** or a **sigmoid-shaped esophagus** predicted **failure**.
Myotomy versus PD

- A randomized trial (201 patients), found similar efficacy for PD and myotomy after two years. (86 and 90%, respectively)

- In some studies myotomy was more effective than PD. (85% versus 65% in long-term follow up. Okike et al.)
Achalasia - treatment options

- The decision between PD and myotomy as initial therapy should be based upon the patient's preferences and on the availability of experienced personnel.
If there is expertise in both procedures, we suggest **pneumatic dilation**.

A dilation-first, myotomy for nonresponders may be the better therapeutic approach.
Surgical myotomy was the most costly strategy.

Although the initial cost was lower for Botox than for surgery, the overall costs were similar by two years.

PD was the most cost-effective treatment strategy over a five-year time horizon.
Late recurrence of dysphagia after myotomy or PD

- Return of tone in the damaged LES muscle
- GERD with peptic stricture formation
- Squamous cell carcinoma of the esophagus
- Endoscopic examination should readily differentiate these disorders.
Endoscopic injection of ethanolamine as a treatment for achalasia

- Moreto treated 33 patients by repeated injection of ethanolamine oleate at LES.

- Mean follow-up: 31.5 months
- Mean of treatment sessions: 3.6

- The result was excellent or good in 31 of the 33 patients after 1 month.
Endoscopic injection of ethanolamine as a treatment for achalasia (cont.)

- This improvement was sustained for more than 2 years.

- None of the patients who were followed-up had to undergo surgery due to failure of the treatment.
Endoscopic injection of **ethanolamine** as a treatment for achalasia (cont.)

- **Complications:**
  - Mild reflux esophagitis (5 cases)
  - Transient thoracic pain (6 cases)
  - Mild fever or chills (5%)
  - Fibrotic stricture (4 cases)
Ethanolamine Oleate in Achalasia

- Ethanolamine oleate in resistant idiopathic achalasia: a novel therapy

- Ramin Niknam, Javad Mikaeli, Narges Mehrabi, et al.

Methods: We evaluated the efficacy of EO in patients that are resistant to or poor candidate of PD and/or cardiomyotomy.

Diluted EO (2.5%) was injected at LES. Injection was repeated at 2 and 4 weeks after first injection.
Results: All patients had good response. (symptom score decreased > 50% and height and volume of barium in TBE decreased > 50%)

The mean symptom score decreased from 11.38 to 3.23 at 1.5 months after the last injection (P = 0.001).
Ethanolamine Oleate in Achalasia

- The mean duration of follow-up was $17.83 \pm 1.12$ months.

- Relapse was observed in six patients; all were re-injected once that proved to be effective.
If the hypothesis of an autoimmune cause were confirmed, topical or systemic immunosuppressive therapy might be worth a trial.

Implanting new inhibitory neurons may provide a cure for achalasia.
The principal activities of the gut, including motility and secretion, are largely controlled by the intramural enteric nervous system (ENS).

The ENS is composed of 80-100 million neurons and many more glial cells.
Enteric neural stem cells (ENSC) are widely distributed in the gut. ENSC may be readily accessible by endoscopic (mucosal biopsy) or minimally invasive surgical techniques.
If stem cells are so ubiquitous in the gut, why does neuronal loss occur at all in some diseases?

This could be due to a defect in the stem cells or a disturbance in the host environment that prevents them from generating new neurons.
**Stem cell transplantation**

- **Local injection** by **endoscopic** or **surgical means**, is the most direct route for localised diseases.

- ENSC can also be delivered **intraperitoneally** or **intravascularly** and may be able to home in to the gut by as yet unidentified cues.
**Stem cell transplantation**

- **NSC transplantation** represents an ideal way to treat **achalasia** in which there is a clearly defined neuronal loss.

- Because ENSCs in other regions of the gut such as the **colon** are not affected, there is a real potential for **autologous transplantation** that alleviate the need for **immunosuppression**.
Peroral endoscopic myotomy

- The key procedures of POEM:
  - Midesophageal mucosal incision
  - Submucosal "tunneling" by endoscopic submucosal dissection
  - Myotomy of the circular muscle at the lower esophageal sphincter
  - Closure of mucosal incision by hemostatic clips
Peroral endoscopic myotomy

- POEM was offered as an alternative to laparoscopic or robotic Heller myotomy
Peroral endoscopic myotomy

- Exclusion criteria:
  - Pregnancy
  - Prior esophageal surgery
  - Immunosuppression
  - Coagulopathies
  - Severe medical co-morbidities
Peroral endoscopic myotomy

- Operative time ranged from **60 to 240 minutes**. *(under general anesthesia)*

- Mean submucosal tunneling length is **12 cm**.

- The average length of endoscopic myotomy is **7 cm**.
CONCLUSIONS:

- As a novel minimally invasive therapy, POEM appears to have definite short-term outcomes.

- POEM significantly reduce dysphagia and resting LES pressure.
Peroral endoscopic myotomy

- **Long follow-up is needed** to evaluate long-term outcome and on comparison of POEM with other therapies.

- **Complications:** submucosal fistula, GERD pneumoperitoneum, Subcutaneous emphysema - **No serious complications**