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Impact of prior treatment on long-term outcome of peroral endoscopic myotomy in pediatric achalasia☆,☆☆

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ABSTRACT

Background and aim: Peroral endoscopic myotomy (POEM) is emerging as an effective treatment for achalasia in children. Long-term outcomes of POEM and impact of prior treatment are not known in pediatric population. In this study, we aim to evaluate the long-term efficacy of POEM in children with achalasia.
Methods: Children (≤18 years) with achalasia who underwent POEM and completed at least 36 months of follow-up were included in the study. Long-term clinical success (Eckardt ≤3) was evaluated and compared between treatment naïve versus prior treated cases.
Results: A total of 53 children underwent POEM at our center during the study period. Of these, 17 children completed at least 3 years of follow-up and were included in the study. Eight children had prior treatment including pneumatic dilatation (6), Heller's myotomy (1) and both Heller's myotomy and pneumatic dilatation (1). POEM was successfully completed in all the children. Median procedure duration was 95.76 ± 47.98 min (38–240 min.). Long-term clinical success was found in 88.2% children. The mean follow-up was 55.06 ± 10.65 months (range 36–67 months). There was no significant difference in the success rate between treatment naïve and prior treatment failure cases.
Conclusion: POEM is a safe, effective and durable treatment for achalasia in children. Prior treatment does not affect the outcomes of POEM in children.
Type of study: Retrospective comparative study.
Level of evidence: III.

Achalasia is a rare neurodegenerative disease characterized by aperistalsis and defective relaxation of lower esophageal sphincter (LES). Pneumatic balloon dilatation (PD) and Heller's myotomy (HM) constitute the mainstay of management in children as well as adult patients with achalasia. However, achalasia is not curable owing to inherent characteristics of the disease. The current treatment options aim to palliate the symptoms of achalasia by reducing the LES pressures.

Recently, peroral endoscopic myotomy (POEM) has emerged as a safe and effective treatment option for achalasia in adult population [1,2]. Preliminary results suggest a good outcome in pediatric population as well [3–7]. However, the data are not as robust in children as compared to adult patients with achalasia mainly owing to the lack of quality evidence on the long-term outcomes of POEM in this population. In addition, the impact of prior treatment has not been evaluated in children. In this study, we aim to evaluate the durability of response to POEM in children with idiopathic achalasia. In addition, we also determined the effect of prior treatment on the feasibility, safety and efficacy of POEM.

1. Methods

The data of children (≤18 years) who underwent POEM for idiopathic achalasia cardia were analyzed, retrospectively. Long-term follow-up was arbitrarily defined as ≥3 years.

The outcomes of POEM including technical and clinical success, procedure duration and complications were compared between treatment naïve and prior treatment failure cases. The study was approved by the institution's review board committee.

1.1. Preoperative evaluation

All the children underwent evaluation using a standardized protocol for achalasia including high resolution esophageal manometry, timed barium esophagogram, and esophagogastroduodenoscopy (EGD). Clinical symptoms were graded according to Eckardt score which is a

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composite of four variables i.e. dysphagia, chest pain, regurgitation and weight loss.

1.2. Technique of POEM

An EGD was performed in all the subjects prior to initiation of POEM procedure to clear the esophagogastric contents. A standard endoscope equipped with water jet (Olympus GIF HQ 190; Olympus Corp., Tokyo, Japan) was used for all the POEM procedures. POEM was performed either via an anterior (1–2 o'clock) or posterior (5 o'clock) route under general anesthesia with the child in supine position. The technique of POEM has been described previously and includes the following steps: submucosal lifting injection, mucosal incision, submucosal tunneling, myotomy and closure of the incision using endoclips [8]. A triangular tip knife (KD-611L/645L, Olympus, Tokyo, Japan) was used for the entire procedure.

The time taken from mucosal injection to the closure of mucosal incision was considered as the operating time. Intraoperative complications were defined as major or minor according to a recent classification proposed by our group [9]. Minor insufflation related adverse events which did not require an intervention were not considered as adverse events.

Capnoperitoneum requiring needle decompression, accumulation of retroperitoneal CO_2 necessitating temporary stoppage of POEM procedure and full thickness mucosal injuries requiring the use of endoclips were regarded as minor adverse events. When required, fluoroscopy was used to differentiate between capnoperitoneum and accumulation of retroperitoneal CO_2.

1.3. Postprocedure care and follow-up

A timed barium swallow was performed on the next day of procedure and oral liquid diet was initiated. Subsequently, a soft diet was allowed for next one week and a regular diet resumed thereafter.

The follow-up was performed at 1 month, 3 months, 6 months, 1 year and yearly, thereafter. At each visit the symptoms of achalasia and gastroesophageal reflux were assessed. Clinical success was defined as Eckardt score ≤ 3. In addition, timed barium swallow, EGD and high resolution manometry were performed for objective evaluation of clinical success.

1.4. Gastroesophageal reflux assessment

Objective assessment of gastroesophageal reflux (GER) was performed with EGD and 24-h pH-impedance study. Reflux esophagitis was graded according to the Los-Angeles grading of severity (grade A to D). A DeMeester score ≥ 14.72 on pH study was considered abnormal.

1.5. Statistics

The data were prospectively collected and comparison of pre- and postprocedure parameters was done in treatment naïve and prior treatment failure cases. Data are presented as mean ± standard deviation. Student's paired t test was used for continuous variables and proportion test for categorical variable. A P-value of <0.05 was considered as statistically significant.

2. Results

2.1. Demographic characteristics

A total of 53 children underwent POEM from March 2013 to April 2019. Of these, 17 children (14.35 ± 3.62 years, 7 boys) completed a minimum of 3 years of follow-up. Majority of the children had type II (58.8%) and type I (35.29%) achalasia. Of these, 8 (47%) of children had history of prior treatment, mainly pneumatic balloon dilatation. The median number of dilatations prior to POEM was 2 (range 1–4). The mean interval between the last dilatation and POEM was 22.87 ± 13.56 months. The baseline Eckardt score and esophageal manometry findings are depicted in Table 1.

Treatment naïve children were significantly older than prior treatment failure cases (16 ± 1.58 vs 12.5 ± 4.44; p = 0.042). Mean pre-POEM integrated relaxation pressures (IRP) were significantly lower in the prior treatment failure group. Other baseline characteristics were similar between both the groups (Table 1).

2.2. POEM procedure details

POEM was performed by an anterior route (1–2 o'clock) in majority of the children (13, 76.47%). A posterior route was utilized in four children including two children with history of prior HM. POEM was technically successful in all the children. The mean operative time was 95.76 ± 47.98 min. Mean operative time was nonsignificantly higher in the prior treatment failure group (Table 2).

2.3. Adverse events

Overall, there were five (29.41%) intraprocedural adverse events including capnoperitoneum (1), accumulation of retroperitoneal CO_2 (3), and mucosal injury (1). Capnoperitoneum was managed with needle decompression in right subcostal space. The procedure was temporarily withheld for 5–10 min in cases of significant accumulation of retroperitoneal CO_2. Mucosal injury was successfully closed using endoclips after the completion of myotomy.

There was no significant difference in the incidence of adverse events between treatment naïve vs prior treatment failure cases (33.3% vs 25%; p = 1.000) (Table 2).

2.4. Clinical success

Clinical success (Eckardt≤3) was noticed in 15 (88.2%) children. Long-term clinical success (55.06 ± 10.65 months) was similar between treatment naïve and prior treatment failure groups (77.8% vs 100%; p = 0.471). Both the clinical recurrences occurred in treatment naïve group.

2.5. Gastroesophageal reflux

Table 1
Demographic characteristics and outcome of children who underwent POEM.

Mean age, years ± SD	14.35 ± 3.62 (range 4–18)
Sex, M/F	7/10
Type of achalasia	
Type I	I=6
Type II	II=10
Type III	III=1
Prior treatment	8
Pneumatic dilatation	6
Heller's myotomy	1
Both pneumatic dilatation and Heller's	1
Eckardt score, mean ± SD	6.88 ± 1.65
Pre-POEM IRP, mean ± SD (mmHg)	23.33 ± 10.87
Procedure duration (minutes)	95.76 ± 47.98
Myotomy type	
Anterior=13	13
Posterior=4	4
Mean follow-up in months	55.06 ± 10.65
Clinical success (Eckardt ≤3)	88.23%
Gastroesophageal reflux	
Grade A and B esophagitis (n = 12)	4 (33.33%)
High De-Meester score > 14.72 (n = 7)	5 (71.43%)

POEM, peroral endoscopic myotomy; IRP, integrated relaxation pressure.

Table 2
Comparison of treatment naïve and prior treatment failure cases.

	Treatment naïve N = 9	Prior treatment failure N = 8	P
Mean age	16 ± 1.58	12.5 ± 4.44	0.042
Pre-POEM Eckardt score	7.11 ± 1.76	6.62 ± 1.60	0.490
Pre-POEM IRP	28.83 ± 12.46	17.20 ± 3.22	0.022
Procedure time	88.89 ± 32.57	103.5 ± 62.62	0.548
Length of myotomy	11.88 ± 1.62	10.12 ± 2.15	0.074
Intraprocedural complications	3 (33.3%)	2 (25%)	1.000
Retroperitoneal CO_2	2	1	
Capnoperitoneum	1	-	
Mucosal Injury	-	1	
Mean follow-up (months)	54.33 ± 11.62	55.87 ± 10.18	0.777
Post POEM IRP	6.57 ± 3.22	8.80 ± 4.52	0.255
Clinical success (Eckardt score ≤ 3)	7 (77.8%)	8 (100%)	0.471
GERD: Esophagitis	2 (n = 6)	2 (n = 6)	1.000
: High De-Meester score	3 (n = 4)	2 (n = 3)	1.000

POEM, peroral endoscopic myotomy; IRP, integrated relaxation pressure; CO_2, carbon dioxide; GERD, gastroesophageal reflux disease.

Erosive esophagitis was detected in 4 (33.33%) children at 1-year follow-up. 24-h pH impedance study was available in seven children. Of these, a high De Meester score (>14.72) was found in 5 (71.4%) children.

3. Discussion

In this study, we found that POEM is a safe and durable treatment option for children with idiopathic achalasia. Prior treatment does not impact the long-term outcomes of POEM in pediatric achalasia.

Achalasia is a rare disease in children and there are no definitive recommendations on the management of pediatric achalasia [10]. The choice of treatment in pediatric achalasia is mainly based on individual preferences and the available expertise. Based on the limited evidence, HM is usually preferred over PD or Botox injection as it provides more durable long-term outcomes [11–13]. However, HM is an invasive procedure and the response to PD and botulinum toxin injection is often not durable.

POEM is a recent addition to the armamentarium of endoscopic treatment modalities for achalasia. There is emerging literature regarding the efficacy of POEM in children [3,5,6,14]. However, the major limitations of these studies are short follow-up duration and lack of objective evaluation. Moreover, the current literature does not describe the impact of prior treatment on the efficacy of POEM in the pediatric age group. Consequently, hesitancy prevails in adopting POEM for pediatric achalasia and HM or PD is preferred over POEM in children with achalasia [12].

In this study, we evaluated the long-term outcomes of POEM in previously treated children with achalasia and compared these with treatment naïve cases. POEM was technically feasible in all the children. There was no significant difference in the operating times and complications between treatment naïve and prior treatment failure groups. This implies that POEM can be safely and effectively performed irrespective of the prior treatment history in pediatric age group. These results are in concordance with the published literature in adult patients [15]. Nevertheless, prior treatment may induce submucosal fibrosis and affect the outcomes of subsequent myotomy including efficacy and complications [16,17].

Clinical success was achieved in majority (100% at 1 year) of the children at 1-year follow-up. Our results confirm the results of previously published studies with short-term follow-up [4,14]. There were two failures in whom POEM was performed in the initial period of our POEM program. As is the case with any new treatment method, it is likely that the results of POEM will improve with experience of the operator.

As compared to previous studies, we focused on the long-term remission rates in these children. There are only two studies which have described relatively long-term outcomes of POEM in pediatric achalasia. However, the average follow-up duration was still short in these studies (13.2 and 24.6 months) [3,5]. Clinical success in these studies was 100% and 96%, respectively. We have previously published short-term outcomes of POEM in children with achalasia [14]. The mean follow-up in the present study was close to four and a half years. A long duration of follow-up is paramount while gauging the efficacy of a treatment modality in achalasia since recurrences are not infrequent in long run. We found a durable response (88%) to POEM at long-term follow-up. Therefore, POEM may be considered as a minimally invasive treatment option for pediatric patients with achalasia.

We also compared the clinical efficacy of POEM in untreated patients versus previously treated children. Prior treatment may affect the outcomes of POEM. In a recent study, the outcomes of POEM were inferior in previously treated adult patients [17]. However, in the present study we found that POEM was equally effective in both the treatment groups. Therefore, POEM may be a good alternative in children who suffer with recurrent symptoms after previous treatment especially pneumatic balloon dilatation.

There are several strengths of the present study. This is the first study which depicts the long term impact of prior treatment on the outcomes of POEM in children with achalasia. The follow-up in this study is longer than the previously published studies. However, we acknowledge certain drawbacks. This is a retrospective study with small number of children who completed at least 3 years of follow-up. In the prior treatment group, majority of the treatment failure children had history of balloon dilatation. Therefore, more data are required before concluding the efficacy of POEM in children who have received Heller's myotomy or botulinum toxin injection as primary treatment.

4. Conclusion

POEM is a durable treatment option in children with achalasia. There is no impact of prior treatment, especially pneumatic dilatation, on the long-term efficacy of POEM.

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