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ORIGINAL ARTICLE

Anesthesia in per-oral endoscopic myotomy: A large tertiary care centre experience

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Abstract

Background and Objectives Per-oral endoscopic myotomy (POEM) is safe and efficacious for the management of achalasia cardia (AC). POEM is usually performed under general anesthesia in an endoscopy suite or operating theatre. The current study was conducted with the aim to analyse anesthetic management of patients with AC who underwent POEM at our institution.

Methods We retrospectively analysed the data of patients with AC who underwent POEM at our institution from January 2013 to September 2016. All cases were performed in an endoscopy suite under supervision of an anesthesia management team. Pre-procedure endoscopic evacuation of esophagogastric contents was done in all cases. Management strategies used for gas-related adverse events and outcomes were assessed.

Results Four hundred and eighty patients (median age 40 years, range 4–77 years) underwent POEM during the study period. The sub-types of AC were type I (163), type II (297), and type III (20). POEM was successfully completed in 97.5% patients. Gas-related events were noted in 30.6% cases including-capno-thorax in 1%, capno-peritoneum in 12.3%, retroperitoneal air in 16.5%, capno-mediastinum in 0.2%, and capno-pericardium in 0.4% patients. Significant rise in end tidal CO2 (> 45) and peak airway pressure were observed in 8.1% and 5.4% cases, respectively. Drainage was required in 12.3% patients. There was no occurrence of aspiration during or after POEM.

Conclusions POEM could be safely performed in an endoscopy suite under supervision of an expert anesthesia management team. Gas-related adverse events were common during POEM and could be managed with a standardized approach.

Keywords Esophageal achalasia · Per-oral endoscopic myotomy · Pneumomediastinum · Pneumoperitoneum · Pneumothorax

Introduction

Achalasia cardia (AC) is a rare esophageal motility disorder defined by aperistalsis and incomplete or absent relaxation of the lower esophageal sphincter [1]. The current treatment options include laparoscopic Heller's myotomy (LHM) and pneumatic balloon dilation (PBD). Botulinum toxin injection and pharmacotherapy are generally reserved for patients who are unfit to undergo either LHM or PBD [2]. Per-oral endoscopic myotomy (POEM) has been introduced recently for the management of AC [3]. Since the first POEM procedure was performed less than a decade ago, the devices and techniques are still evolving. The published literature suggests excellent safety and short-term outcomes with POEM [4–7].

POEM is performed under general anesthesia either in an operating theatre or an endoscopy suite depending on the institutional preference. There are unique anesthetic management challenges in patients with AC undergoing POEM. Pulmonary changes like restrictive airway disease are common in patients with AC [8, 9]. Moreover, since the endoscopist works in sub-mucosal space with frequent exposure of mediastinum, gas-related events like subcutaneous emphysema, retroperitoneal air, pneumoperitoneum and pneumothorax are frequent intraoperative events during POEM [10–13]. In such cases, the management of ventilation

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is important to avoid the transformation of 'events' into 'adverse events'. The literature on anesthesia management during POEM is sparse, and current practice is based on individual experiences and preferences [14–16]. In this study, we retrospectively analysed the anesthetic management of all the cases of AC who underwent POEM at our institution.

Methods

All the patients with AC who underwent POEM at our institution from January 2013 to September 2016 were analysed, retrospectively. Informed consent was taken from all the patients.

Pre-POEM evaluation

A standard pre-anesthetic evaluation was performed for all the patients who underwent POEM and included complete hemogram, renal function tests, liver function tests, thyroid function tests and pulmonary and cardiac evaluation. In addition to the above tests, gastroscopy was performed in all the patients prior to POEM to look for esophageal candidiasis and ulceration due to stasis esophagitis. In subjects with esophageal candidiasis, oral antifungals were given for 1 to 2 weeks prior to the procedure.

The contraindications to POEM procedure were coagulopathy, significant cardiorespiratory dysfunction, portal hypertension with esophageal varices, previous irradiation to chest wall and small children <15 kg.

Prior to POEM procedure, the diet of patients was modified for 36 h prior to procedure—clear liquids for the first 24 h and nothing by mouth for last 12 h before the procedure. In cases with history of significant solid food residue on index endoscopy and those with sigmoid esophagus, instruction for clear liquids were given for 72–96 h before the POEM procedure.

Pre-POEM medications

All the patients received pre-procedure intravenous antibiotics (Piperacillin-Tazobactum 4.5 g) and proton pump inhibitors (equivalent to 40 mg pantoprazole).

Gastroscopy was done with a large channel endoscope under light sedation in all the cases about half an hour prior to POEM procedure to evacuate residual esophageal and gastric contents.

Mechanical ventilation details

POEM procedure was performed in supine position under general anesthesia. Tracheal intubation was done after induction with intravenous Propofol and Atracurium besylate (0.4–0.5 mg/kg) as muscle relaxant. The dose of Propofol was based on age as follows: 2.5–3.5 mg/kg in children <18 years, 2–2.5 mg/kg in <55 years and 1–1.5 mg/kg in >55 years age group. A cuffed flexo-metallic endotracheal tube (to prevent kinking or compression of endotracheal tube) was used in all the cases.

Volume-controlled positive pressure ventilation was utilized in all the cases. The usual ventilator settings were positive end expiratory pressure (PEEP) of 5–8 cm H2O, tidal volume of 5–8 ml/kg, respiratory rate 12–14/min, inspiratory/expiratory ratio of 1:2 to 1:3 and fraction of inspired oxygen (FiO2) of 50%. Anesthesia was maintained by 50% oxygen and 50% air, and sevoflurane (0.5–2 minimum alveolar concentration) was titrated to keep the bispectral index scale values between 40 and 50.

Dexmedetomidine hydrochloride infusion (1 mcg/kg loading infusion over 10 min, followed by maintenance infusion of 0.2–0.7 mcg/kg per hour) was administered for the period of POEM procedure. Intermittent doses of low-dose fentanyl (2 mcg/kg) was used for analgesia.

POEM procedure—technique

We have elucidated the technique of POEM procedure in detail in our previous studies [4, 17]. Upper gastrointestinal gastroscope equipped with auxiliary water jet function (Olympus GIF HQ 190; Olympus Corp., Tokyo, Japan) was used for all the procedures. A transparent tapered end cap (DH-28GR; Fujifilm, Tokyo, Japan) was fitted onto the distal end of gastroscope. The steps of POEM procedure were as follows: (1) creation of a submucosal bulge by injecting solution (saline and indigo-carmine dye) at about 10–15 cm above gastroesophageal junction, (2) making a small incision over the bulge with needle knife and enlarging it using insulated tip knife, (3) clearance of fibres beneath the edges of mucosal incision and entry into the future tunnel, (4) creation of submucosal tunnel using triangular tip knife, (5) selective circular myotomy in the upper part of tunnel and full-thickness myotomy from 2 to 3 cm above GE junction till the end of tunnel and (6) closure of mucosal incision with endoclips (EZ Clip, HX-610-090L, Olympus, Japan) (Fig. 1).

Minor blood ooze during the procedure was controlled using triangular tip knife (Triangle Tip Knife, KD-640L, Olympus, Japan), while significant bleeding was managed with coagrasper (Coagrasper G, FD-412LR, Olympus, Japan) in soft coagulation mode (80 W, effect 5). The entire POEM procedure was performed under carbon dioxide (CO2) insufflation using an extra low flow gas tube (MAJ-1816).

Intra-operative ventilation monitoring

The components of intra-operative monitoring included heart rate, electrocardiogram, non-invasive blood pressure, oxygen saturation and peak airway pressure. In addition, end tidal CO2 (etCO2) and peak airway pressure were closely

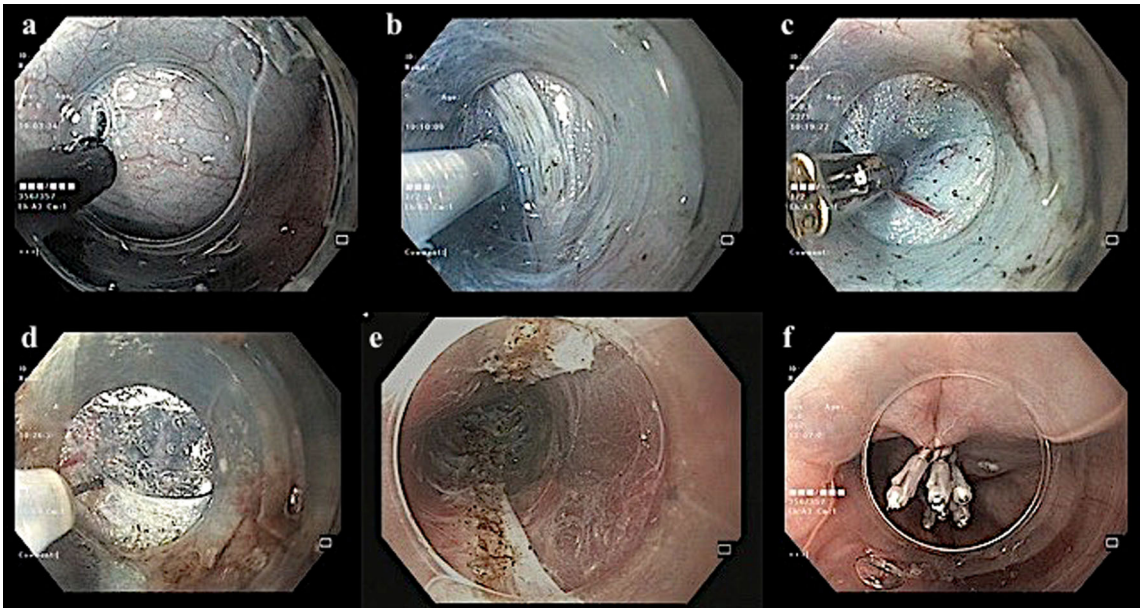

Fig. 1 Steps of per-oral endoscopic myotomy. **a** Sub-mucosal injection followed by mucosal incision. **b** Sub-mucosal tunnelling using triangular tip knife. **c** Coagulation of intervening blood vessel with coagulation forceps. **d** Myotomy using triangular tip knife. **e** Completion of myotomy. **f** Closure of mucosal incision with endoclips

monitored throughout the procedure. etCO2 was kept between 35 and 45 mmHg while peak airway pressure below 30 mmHg.

Management of intra-operative gas-related events

Gas-related events were identified clinically and confirmed fluoroscopically when necessary. Initially, the rise in etCO2 was managed by adjusting ventilator settings, i.e. increasing the PEEP from 5 to 10 cm H2O (depending on the pulmonary status), increasing the respiratory rate and giving 100% oxygen in the fresh gas flow to wash out the CO2.

Subsequently, the decision to intervene further was based on degree of rise in etCO2, peak airway pressure and clinical judgement (anesthesiologist and endoscopist). In cases of capno-peritoneum with significant rise in etCO2 (> 50), needle decompression was done using an 18G intravenous cannula in the anterior axillary line below the right costal margin. The procedure was paused for 10–15 min in cases of retroperitoneal CO2 along with significant abdominal distension. In both capno-peritoneum and retroperitoneal CO2, POEM procedure was resumed after subsidence of abdominal distension and return of etCO2 and peak airway pressures to baseline.

Capno-thorax and capno-mediastinum were identified clinically by reduced chest wall excursion on the affected side and increased airway resistance. The procedure was paused and drainage performed in cases of deterioration of vital parameters or fall in etCO2 suggestive of significant airway compromise. In addition, ventilation with 100% O2 was carried.

Definitions

Technical success was defined as successful completion of the procedure. Clinical success was defined as improvement in clinical symptoms, i.e. Eckardt score ≤3. Adverse events were defined as those requiring a specific intervention like insufflation-related events requiring drainage or transiently withholding the procedure and those leading to prolonged hospitalization. Intra-procedural minor bleeding episodes and subcutaneous emphysema were not considered as adverse events.

Post-procedure management

All the patients were kept nil per oral for 1 day after the procedure. Thin barium esophagogram was done on the second post-operative day to look for any leak. The patients were started on liquid diet on day 2 and soft diet from day 3 onwards.

Post-POEM hematological (hemoglobin and white blood cell count) and biochemical parameters (blood urea nitrogen, serum creatinine and serum sodium/potassium) were recorded and compared with pre-POEM values.

Statistics

The data is presented as mean standard deviation or median. Student's paired *t* test was used for continuous variables and proportion test for categorical variables. *P*-value <0.05 was considered statistically significant.

Results

Patient characteristics

A total of 480 patients (median age 40 years, range 4–77 years, 269 males) with AC underwent POEM in our department during the study period (January 2013 to September 2016) (Table 1). According to Chicago classification, the sub-types of AC were type I (n = 163), type II (n = 297), and type III (n = 20). Two hundred and thirty-six patients (49.2%) had history of prior treatment failure including PBD (202), LHM (21), LHM and PBD both (6), botulinum toxin injection (4) and POEM (3).

Procedure characteristics (Table 2)

POEM could be successfully performed in 468 (97.5%) patients. Mucosal incision enlargement (3 patients) and excessive submucosal fibrosis (9 patients) were the primary reasons for abandoning the procedure.

An anterior approach (~ 2 o'clock) was used in majority of the patients (383/480; 79.8%), whereas 97 (20.2%) patients underwent POEM via posterior approach (~ 5 o'clock position). All patients who had previously undergone LHM were treated with posterior myotomy.

The mean time of POEM procedure was 72.6±28.9 min (30 to 180 min). Median length of total myotomy was 13 cm (range 6–21). The median length of myotomy on esophageal and gastric side was 10 cm (range 3–18) and 3 cm (range 1–4), respectively.

Peri-operative adverse events

Intra-operative adverse events included gas-related (capno-peritoneum, retroperitoneal CO2, capno-thorax, capno-mediastinum and capno-pericardium) and inadvertent mucosotomies (Fig. 2). There was no event of CO2 embolism or compartment syndrome. Overall, gas-related adverse events were noted in 30.4% patients. There was no difference in gas-related adverse events in anterior vs. posterior POEM (31.8% vs. 24.7%, p-value 0.22).

Rise in etCO2 (> 45) was observed in 39 patients (8.1%), whereas peak airway pressure elevation was found in 26 patients (5.4%).

Capno-peritoneum requiring temporary cessation of procedure along with adjustments in ventilator settings (increase in respiratory rate and or tidal volume) and needle decompression (18G intravenous cannula) occurred in 59 (12.3%) patients.

Retroperitoneal CO2 accumulation requiring a 'procedure pause' and modifications in ventilator parameters was observed in 79 (16.5%) patients.

Insufflation-related pulmonary events were noticed in 8 patients including capno-thorax in 5 (1%), capno-mediastinum in 1 (0.2%) and capno-pericardium in 2 (0.4%) patients. Capno-thorax was identified clinically by limited excursion of chest wall on the affected side and confirmed by fluoroscopy which revealed moderate-sized pneumothoraces. We paused the procedure for about 15 min following which all resolved, and none required a drainage procedure.

Table 1 Demographics of patients undergoing per-oral endoscopic myotomy

No. of patient	480
Mean age, years (+SD, range)	40.25±13.68 (4–77)
Male: female	269:211
Types of achalasia	
Type I	163
Type II	297
Type III	20
Previous therapy	
Botulinum toxin inj.	4
Pneumatic balloon dilatation	202
Heller's myotomy	21
PBD and LHM	6
POEM	3

PBD pneumatic balloon dilation, *LHM* laparoscopic Heller's myotomy, *POEM* per-oral endoscopic myotomy

Table 2 Operative findings, adverse events and postoperative follow up

Operating time (min) Mean±SD (range)	72.56±28.96 (30–180)
Site of myotomy	
Anterior	383 (79.8%)
Posterior	97 (20.2%)
Length of myotomy (cm)	13 (6–21)
Esophageal (cm)	10 (3–18)
Gastric (cm)	3 (1–4)
Adverse events	
Mucosal injury	18 (3.7%)
Significant bleeding	0
Gas related events	
Subcutaneous emphysema	96 (20%)
Gas related adverse events	
Capno-thorax	5 (1%)
Capno-peritoneum	59 (12.3%)
Retroperitoneal air requiring temporary stoppage of procedure	79 (16.5%)
Capno-mediastinum	1 (0.2%)
Capno-pericardium	2 (0.4%)
Pleural effusion	1 (0.2%)
No. of clips, median (range)	6 (3–22)
Technical success	468/480 (97.5%)
Hospital stays, mean (range)	3 (2–5 days)
30-day readmission rate	1 (bronchopneumonia)

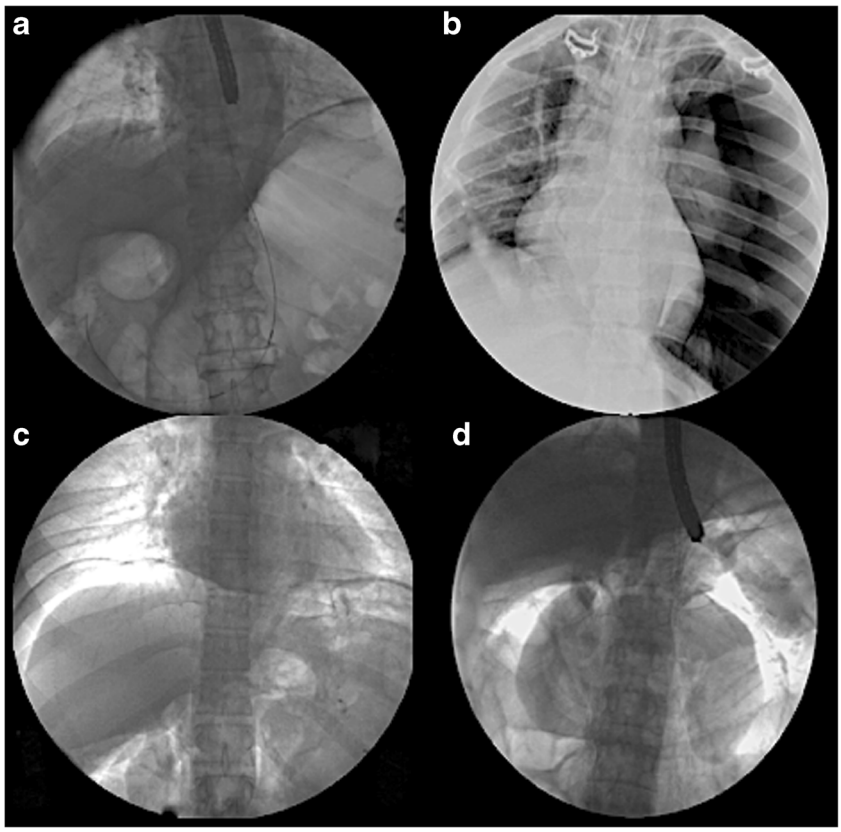

Fig. 2 Gas-related adverse events during per-oral endoscopic myotomy. **a** Excessive gastric distension leading to distension of abdomen. **b** Left-sided capno-thorax requiring temporary cessation of procedure. **c** Gas under diaphragm suggestive of capno-peritoneum. **d** Retroperitoneal CO2—note gas outlining both the kidneys

Capno-pericardium was observed in two cases. In both the cases, POEM was being performed via an anterior approach. In the first case, it was detected incidentally on fluoroscopy which was being performed to confirm extension of tunnel across gastroesophageal junction. In the second case, sudden hypotension and desaturation was observed and fluoroscopy revealed thin rim of air around heart. In both the cases, the procedure was paused for about 30 min. Subsequently, the procedure was completed successfully.

Subcutaneous emphysema was observed in 96 cases (20%). However, it was not considered as an AE as no specific intervention was required.

One patient was readmitted within 4 weeks of procedure for fever and shortness of breath. Evaluation revealed bronchopneumonia and leukocytosis. This patient responded to intravenous antibiotics.

There was no occurrence of aspiration, major intra-operative bleeding requiring blood transfusion, delayed bleed and post-operative leak or mediastinitis.

Post-operative parameters

All the patients were successfully extubated after general anesthesia in the endoscopy suit. There was significant reduction in heart rate (78.17±8.01 vs. 60.43±8.37; *p*-value 0.0001) and systolic blood pressure (112.67±9.90 vs. 100.73±9.61) which persisted on day 1, but not day 2 of the procedure (Table 3).

Complete blood picture revealed significant reduction in hemoglobin (12.86±1.90 vs. 11.04±1.96; *p*-value 0.0001) along with significant rise in white blood cell count (7936.67±2722.32 vs. 9431.46±2615.50; *p*-value 0.0001) on day 2 of the procedure. A significant reduction in blood urea nitrogen (day 2) was also observed after the procedure. There was no significant change in serum creatinine, serum sodium and serum potassium (Table 3).

Discussion

In this study, we conclude that POEM can be safely performed in an endoscopy unit under the supervision of an expert anesthesia management team.

POEM is arguably the most rewarding wing of Natural Orifice Transluminal Endoscopic Surgery (NOTES) with excellent safety and short-term efficacy [4, 18–20]. The literature is divergent regarding the learning curve of POEM [21–23]. Nevertheless, the procedure is technically demanding and as the endoscopist operates in critical areas, optimal patient sedation is mandatory. Almost universally, POEM is carried out under general anesthesia supervised by an expert anesthesiologist. There are limited studies regarding anesthesia management and mechanical ventilation in POEM [14–16, 24].

Table 3 Comparison of pre- and post-POEM parameters—vitals, haematologic and biochemical

	Pre-POEM	Post-POEM	*p*-value
Pulse rate per min. (mean of median)	78.17±8.01	60.43±8.37[b]	0.0001
Blood pressure (mmHg)	112.67±9.90	100.73±9.61[a]	0.0001
Hemoglobin (g/dL)	12.86±1.90	11.041.96[b]	0.0001
WBC count (g/dL)	7936.67±2722.32	9431.46±2615.50	0.0001
Blood urea nitrogen (mg/dL)	21.96±6.59	17.57±5.42[b]	0.0001
Creatinine (mg/dL)	0.82±0.17	0.83±0.19	0.08
Serum sodium	137.68±2.32	137.77±1.73[b]	0.49
Serum potassium	3.95±0.32	3.92±0.38	0.19

[a] Day one of procedure

[b] Day 2 of procedure

The role of anesthesia management team is challenging in patients with AC undergoing mechanical ventilation due to a multitude of factors. Primarily, subjects with AC have frequent pulmonary symptoms and pulmonary function tests often reveal restrictive airway disease [8, 9]. Secondarily, these patients have significant esophageal stasis with risk of aspiration. Therefore, strategies to prevent aspiration are important. Thirdly, the gas-related events are frequent during POEM [10, 12, 13]. Although most of these events are inconsequential, changes in mechanical ventilation parameters may be required to increase minute ventilation and speed up CO2 washout.

We performed all the cases under general anesthesia with the patient in supine position. Endoscopic aspiration of esophageal and gastric contents was performed in all the cases under light sedation prior to induction of general anesthesia. With this approach, we did not encounter aspiration in any of our cases. Although uncommon, aspiration has been described during POEM procedure and experts recommend an endoscopy prior to general anesthesia to aspirate esophagogastric contents. Alternatively, rapid sequence induction with cricoid pressure and intubation in semi-reclined position can be done to minimize aspiration [15]. Some centres use specially designed endotracheal tube which has an evacuation port and suction lumen (TaperGuard Evac, Covidien, Mansfield, MA) to facilitate drainage of subglottic secretions [24]. With rapid sequence technique, a recent study concluded that prior endoscopic esophageal content clearance is not required to prevent aspiration. The patients were kept on a clear liquid diet for longer period (2–5 days) in that study [15]. However, in our experience, residual contents in esophagus may be found in some cases especially those with grossly dilated or sigmoid esophageal configurations even after several days of clear liquid diet.

Emerging data suggests that POEM can be safely performed in an endoscopy suit [15, 20]. In our study, all the POEM procedures were successfully performed in an endoscopy suit. None of the cases had to be shifted to operation theatre in lieu of serious adverse events. In the near future, the shift of POEM procedure from operation theatre to endoscopy suit is anticipated worldwide owing to excellent data on its safety.

We performed all the POEM procedures under general anesthesia after standard induction protocol. Although POEM can be performed under deep sedation, it is not advocated since patient movements can be detrimental. Moreover, the length of procedure can be unpredictably long on occasions with obvious difficulty and risk of maintaining sedation. In a recent study, the frequencies of adverse events were higher when intravenous anesthesia was used for POEM procedure [25].

As the procedure is performed under general anesthesia with frequent gas-related adverse events, an expert anesthesiologist is required to monitor patient's ventilation for the entire duration of procedure. In POEM, the endoscopist works in submucosal or the 'third space' in close vicinity of mediastinal or peritoneal space. Therefore, gas readily penetrates the muscular layer and leads to various gas-related events like pneumo-thorax, pneumo-peritoneum, subcutaneous emphysema and rarely pneumo-pericardium. In our study, gas-related adverse events were noticed in 30.6% cases. There was no difference in gas-related adverse events in anterior and posterior approaches to POEM. Similar incidence of gas-related adverse events has been described in some of the recently published studies [10]. The recognition of insufflation-related adverse events in our study was based on clinical judgement, increased airway resistance and etCO2 which served as a surrogate marker for hypercapnia. Fluoroscopy was used when deemed necessary. Fortunately, most of the gas-related events do not lead to clinically significant consequences. The strategies to prevent insufflation-related events are manifold. The most important ones include using CO2 for insufflation and positive pressure mechanical ventilation. The absorption of CO2 is much faster than air and has virtually replaced air for insufflation in most of the gastrointestinal procedures. In a large study, intraoperative gas-related events reduced significantly after shifting from air to CO2 [11]. In addition, efforts to minimize insufflation while

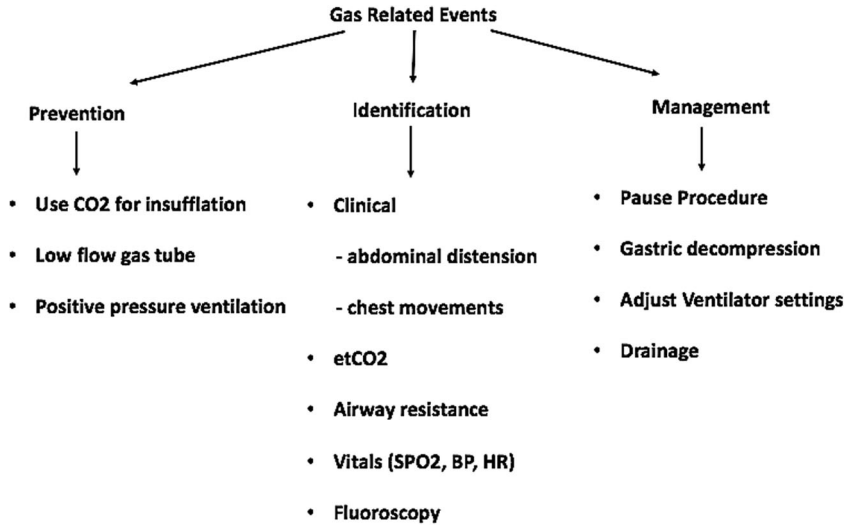

Fig. 3 Approach to the management of gas related adverse events

working in submucosal tunnel and use of low flow gas tube may further reduce insufflation-related adverse events [26]. However, randomized trials are lacking.

The management of gas-related adverse events largely depends on the compartment affected and hemodynamic consequences if any. In our study, we utilized a four-pronged approach for the management of insufflation-related complications (Fig. 3). These included gastric decompression, temporary pausing the procedure to allow CO2 absorption, subtle changes in ventilator settings to increase minute ventilation and augment CO2 wash out and lastly needle decompression in that order. With this approach, none of the capno-thoraces required drainage procedure. Small pneumothoraces can be safely observed, whereas larger ones may lead to cardiovascular compromise and should be drained without delay.

We encountered two instances of capno-pericardium in our study. Both the cases were successfully managed with pausing the procedure in addition to the ventilation adjustments as mentioned above. However, capno-pericardium may result in grave consequences and the decision to proceed with the procedure has to be judicious. In a recent report, tension capno-pericardium resulted in atrial fibrillation and cardiac arrest and the POEM procedure had to be aborted [27]. In contrast to this case where tension capno-pericardium was detected during tunnelling and associated with loss of pulse and blood pressure, we noticed capno-pericardium during myotomy near completion.

The drainage procedure was only performed for clinically significant capno-peritoneum associated with substantial abdominal distension and or rise in etCO2. In none of the subjects, the procedure had to be abandoned due to insufflation-related consequences.

We observed one case of bronchopneumonia requiring re-hospitalization and one mild pleural effusion. Sub-segmental atelectasis can occur in the postoperative period. Anesthetic agents, narcotics and splinting due to postoperative pain/discomfort are common causes. Sparing use of narcotics and incentive spirometry can help prevent these adverse events.

We also compared pre- and post-POEM hematological, biochemical and vital parameters (heart rate and blood pressure). There was significant reduction in post-POEM hemoglobin. Patients with AC are often hypovolemic as evident by significant fall in blood urea nitrogen after intravenous fluids in our study. Hemodilution can therefore lead to fall in hemoglobin as observed in our study. Significant elevation of white blood cell count as compared to pre-POEM counts was also observed after POEM. Increase in leukocyte counts is not unusual after stress or tissue trauma and is a consequence of inflammatory cytokines as an acute phase response [28].

The fall in blood pressure and heart rate observed in the current study is explained by intra-operative drugs used during general anesthesia (Fentanyl, Propofol, Sevoflurane, Dexmedetomidine). All the aforementioned changes are inconsequential and prior knowledge would avoid unnecessary investigations.

POEM can be safely performed in an endoscopy suit under supervision of an expert anesthesia management team. Gas-related adverse events are common during POEM and demand close monitoring of ventilation. Fluoroscopy during POEM is a useful aid in confirming the gas-related AE and helps in taking appropriate action when required.

Compliance with ethical standards

Conflict of interest SD, ZN, MR, RC, RK, and DNR declare that they have no conflict of interest.

Ethics statement The authors declare that the study was performed in a manner to conform to the Helsinki Declaration of 1975, as revised in 2000 and 2008, concerning Human and Animal Rights.

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