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Efficacy of Intraoperative, Single-Bolus Corticosteroid Dose to Prevent Postoperative Respiratory Complication after Transhiatal Esophagectomy

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ABSTRACT

Introduction: Esophageal cancer is among the most common malignancies. Hospital mortality in the past decade reduced; but its morbidity is still high. Pulmonary complications are the most common complications after esophageal resection. In this study we examined the effect of steroids administration during surgery to reduce postoperative morbidity with a focus on respiratory complications.

Material and Methods: Patients with esophageal cancer who underwent transhiatal esophagectomy, randomly divided into two groups to thirty patients: The intervention group (received 125mg methylprednisolone sodium succinate).

After surgery, patients admitted in the ICU for a day. Oral feeding initiated on day 7th and patients discharged home on the day 8th or 9th.

Postoperative complications included anastomotic fistula, wound infection in the neck and abdomen and pulmonary complications. We analyzed pulmonary complications included pneumonia, Acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) occurred before the seventh day. The leukocyte counts and CRP levels measured on the 2nd and 7th days after surgery.

Results: 60 patients enrolled in the study. Incidence of ARDS, ALI and pneumonia in the control group was 3, 5 and 2 and in steroid group 1, 1 and 1 respectively. CRP levels and blood leukocyte count was similar in two groups on the second day but seventh day values and difference between the two levels between the second and seventh days were significantly different between the two groups ($p<0.001$).

Conclusion: Intraoperative single dose corticosteroids are effective in preventing pulmonary complications after transhiatal esophagectomy. Methylprednisolone reduced the increase in CRP levels after surgery and decreased blood leukocyte count more in postoperative period.

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Introduction

Esophageal cancer is one of the most common malignancies all around the world.

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The most common histology of esophageal cancer is squamous cell carcinoma, although esophageal adenocarcinoma is increasing. (1) Nevertheless recent progression in multi-modality treatment, esophageal cancer is a lethal neoplasm with a poor prognosis, although in the last decade, diagnostic strategy and clinical staging has improved obviously. One of the most important revolutions has occurred in the management of esophageal cancer and different options include surgery, induction chemotherapy and surgery followed, definitive chemotherapy or radiotherapy and palliative measures are elected according to clinical staging. Surgery has an important role in the treatment of benign and malignant disease of the esophagus. Along last decade, hospital mortality after esophageal resection has been reduced dramatically but still this procedure associates with high morbidity that respiratory complications are one of the most common (2, 3). Respiratory complications include atelectasia, pneumonia and respiratory failure results in high morbidity and mortality after esophagectomy that its true incidence is between 35% to 47%.(4) Release of inflammatory cytokines after surgery is one of the posed hypothesis contributing to respiratory complications.(5)Multiple studies constructed to show efficacy of perioperative corticosteroids to reduce these cytokines and reduction of inflammatory response after surgery and some of them showed efficacy (6, 7). In this study we evaluate the efficacy of single bolus dose of intraoperative corticosteroid on reducing inflammatory response and also respiratory complications after transhiatal esophagectomy.

Materials and Methods

We performed a clinical trial study of patients admitted to thoracic surgery ward of Qaem hospital (2014-2015), Mashhad, Iran with esophageal cancer regardless of pathology. All data collected in a prospective manner. Indication of esophagectomy was esophageal cancer in all patients. Patients who had appropriate indication for transhiatal esophagectomy were elected and those who need neoadjuvant therapy or three hole esophagectomy excluded from study. Preoperative staging performed by chest and abdominal CT scan, endoscopic ultrasound with or without PET scan. 30 patients emerged into every group. Patients who met the inclusion criteria single blinded and randomize (by a person out of the research group) divided into two groups (Even and odd). Group one who didn't receive corticosteroid (Control group) and group two with administration of 125 mg methyl prednisolone sodium succinate at the end of esophagogastric anastomosis (steroid group). The informed consent was obtained from all these patients. Reconstruction accomplished by gastric pull up in all cases. Anastomosis performed in a single layer with 3-0 silk material to the anterior of stomach. Routinely we inserted right sided chest tube with feeding jejunostomy tube. All patients transferred to ICU post operation and if with no complication, they transferred to surgery ward on the first or second postoperative day unless they encountered respiratory problems. Jejunostomy feeding started on second postoperative day and barium swallow examination performed on POD6. P.O (per os) feeding started gradually after taking swallow radiograph. All complication registered strictly. Leukocyte count and CRP level measured on POD2 and POD7 and compared between two groups. Respiratory complications include Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), pneumonia after surgery analyzed by pulmonologist (The day of admitted in ICU) according to its own specific criteria. Abnormal chest X-ray with new consolidation, fever with no other detectable origin and productive cough point the diagnosis of pneumonia. In this setting we performed smear and culture of the sputum with antibiogram, bronchoscopy with BAL, then started empiric antibiotic therapy against pseudomonas and acinetobacter. ALI is defined as an acute lung disease with bilateral pulmonary infiltrate in chest radiograph consistent with the presence of edema with no clinical evidence of left atrial hypertension. ARDS, the most severe form of ALI has five characteristic including abrupt onset, predisposing factor, PaO2/FiO2 less than 200 mmHg, bilateral lung infiltration, no clinical evidence of associated with right side heart failure. So, bronchoscopy with BAL, smear & culture with antibiogram, ABG, chest X-ray and echocardiography performed to evaluate respiratory complication after surgery. All data analyzed by SPSS version 12. The current study is approved in regional ethic committee of Mashhad University of Medical Sciences and the proposal code is 921170. Also we have registered this clinical trial in IRCT and the Registration ID in IRCT is RCT201710092517N3.

Results

The mean age of the patients was 59.85±8.12 years and there were 34 women and 26 men. There were 30 patients in every group. (Table 1)

Patients' demographic characteristics were not different between two groups. Respiratory events occurred in 13 patients during their hospitalization (21.67%). In the control group, there were 5 patients with ALI, 3 with ARDS and 2

Table 1. Baseline characteristics of patients

	group	number	percentage	P value
History of pulmonary disease	intervention	7	23.33%	0.166
	Control	3	10%	
	total	10	16.67%	
smoking	intervention	3	10%	0.278
	Control	6	20%	
	total	9	15%	
diabetes	intervention	4	13.33%	0.389
	Control	2	6.67%	
	total	6	10%	
History of coronary disease	intervention	3	10%	0.99<
	Control	3	10%	
	total	6	10%	
History of renal disease	intervention	0	0%	-
	Control	0	0%	
	total	0	0%	
History of blood pressure	intervention	12	40%	0.417
	Control	9	30%	
	total	21	35%	

The Chi-Square Test was used, the p-value <0.05 is significant.

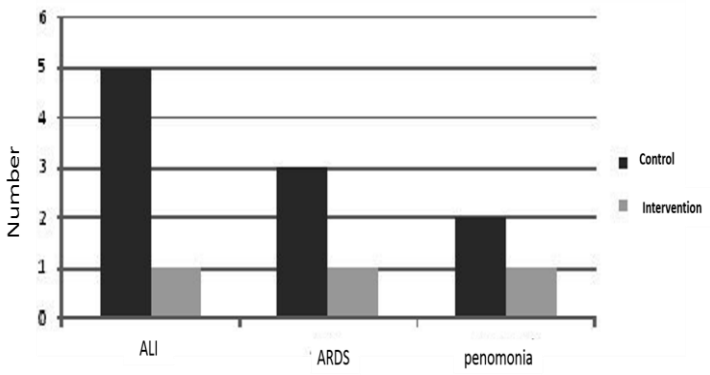

Figure 1. acute pulmonary complications in patients

patients with pneumonia. In the steroid group, there was one patient with ALI, one with ARDS and one patient with pneumonia. The incidence of acute respiratory failure was lower in the steroid group than in the control group (P=0.020). (Figure 1) One wound infection occurred in every group that in control group wound infection was due to fistula in the neck. There was no significant difference between two groups. There was no mortality in our patients. The mean CRP level in POD2 was 1.37±1.13 in control group and 1.67±0.92 in steroid group. In POD7 the measured CRP level increased in both groups but rise in the steroid group was lower (P=0.001). Also the difference between CRP level in POD7 was significant between two groups (P=0.001). Leukocyte count in POD2 was 9860±2551.35 in control group and 13400±4013.61 in steroid group. Leukocyte count in POD2 was 9860±2551.35 in control group and 13400±4013.61 in steroid group. In POD7 leukocyte count was 9146±4316.91 in control group and 7436±3024.78 in steroid group. Difference of leukocyte count in POD2 and POD7 and also difference of leukocyte count in POD7 between two groups were significant (P=0.001). (Figure 2, 3) Despite reduction in respiratory complication, there was no significant effect of

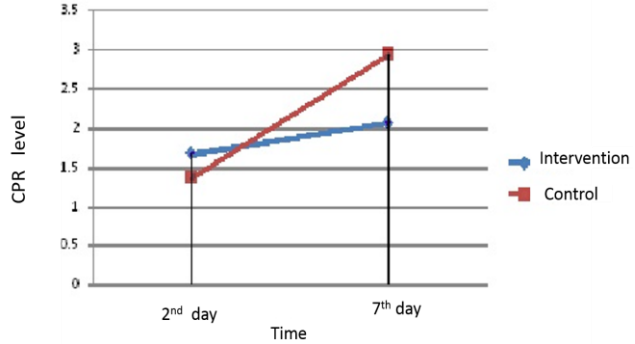

Figure 2. CRP level in study groups

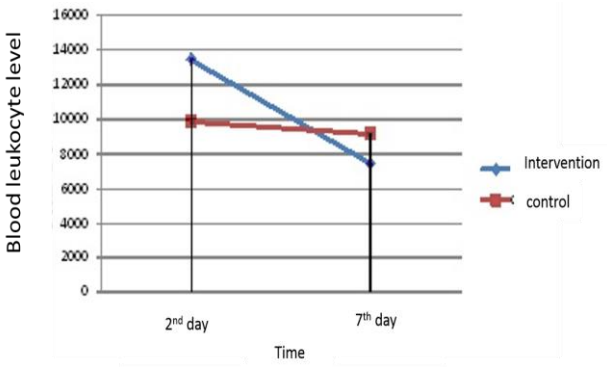

Figure 3. Blood leukocyte level in study groups

steroids on wound healing and wound complications.

Discussion

Major operations like esophagectomy can start inflammatory response and produce cytokines may result in complications that some of them like respiratory failure can be catastrophic. (5, 8) Bailey and coworkers published their investigation on outcome of patients after esophagectomy in 2002.They analyzed 1777 patients in 199 centers. All complications during admission and 30 days follow up recorded.30 days' mortality was 9/8%.They registered twenty different complications and one or more complications seen in 49/5% of their patients. Pneumonia was the most common with the incidence of 21%. Other respiratory complications included respiratory failure (ARDS&ALI) in 16%, prolonged ventilation after 48h in 22% and unprogrammed intubation in 16/2% of cases. Respiratory complications occurred in 21/67% of our patients and the results were similar to Bailey's study. (2) Respiratory complications after esophagectomy increase mortality up to fourfold. According to Tendon and associates, incidence of ARDS is 14/5% with 50% mortality. (3) Different factors affect on respiration postoperatively. Minimally invasive surgery, postoperative physiotherapy, blood loss during surgery and need for transfusion, thoracotomy and use of corticosteroids all investigated. (9) There are also different studies that analyzed immune system modulator to reduce inflammatory response. (10,11,12,13)

Although results were inconsistent in different reports, but many could show the effectiveness of low dose corticosteroids. Our study constructed a homogen group with the same demographic characteristic between control and steroid groups and we excluded the patients who need three hole esophagectomy and also neoadjuvant therapy to eliminate the effect of thoracotomy and radiation on lung function. Although we didn't measure other markers of inflammation (IL1-IL6-IL8-IL10, lymphocyte and neutrophil), but this study showed that administration of single prophylactic dose of corticosteroid intraoperative can be associated with reduction in postoperative inflammatory response. So this can modulate one of the posed hypotheses in creation of post esophagectomy respiratory failure. More prospective studies with more cases and even meta-analysis is needed to prove the effect of steroids on postoperative respiratory complications.

Conclusion

Preoperative single dose corticosteroids are effective in preventing pulmonary complications after transhiatal esophagectomy. Methylprednisolone reduced the increase in CRP levels after surgery and decreased blood leukocyte count more in postoperative period.

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Conflict of Interest

The authors declare no conflict of interest.

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