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Alimentary Tract

Effect of perioperative steroid therapy on the postoperative course of patients with oesophageal cancer

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Abstract

Background. Perioperative steroid therapy is often used in oesophageal cancer surgery and we evaluate the effect of this therapy on the secretory leukocyte protease inhibitor levels in the lungs (a major antiprotease in the conducting airways) and postoperative course in oesophageal cancer patients.

Methods. Twenty-one patients operated on for oesophageal cancer in 2003–2004 were treated with perioperative steroid therapy (250 mg of methylprednisolone intravenously 1 h before the operation). Fifteen consecutive patients operated on in 2002 served as a control group. Secretory leukocyte protease inhibitor in bronchoalveolar lavage fluid and the postoperative course in the two groups were compared.

Results. The mortality rate was 0% and there was no significant difference in the morbidity rate between the two groups. Days of intubation and systemic inflammatory response syndrome were significantly shorter for the steroid group. The bronchoalveolar lavage fluid secretory leukocyte protease inhibitor level was significantly higher in the steroid group than in the control group on postoperative days 2 and 3. The secretory leukocyte protease inhibitor level on postoperative day 3 was remarkably lower for the patients intubated for ≥5 days and for those with pulmonary complications.

Conclusion. Perioperative steroid therapy increased the bronchoalveolar lavage fluid secretory leukocyte protease inhibitor level and reduced the days of intubation and systemic inflammatory response syndrome in patients with oesophagectomy.

Keywords: Oesophageal cancer surgery; Secretory leukocyte protease inhibitor; Steroid therapy

1. Introduction

Oesophageal cancer surgery is known to be one of the most stressful procedures among all gastrointestinal operations [1–4]. In spite of recent improvements in surgical techniques and perioperative care, the postoperative mortality rate was reported to be still 2–12.3% [5–7]. In addition, severe postoperative complications, such as infection, pulmonary complications and liver dysfunction required extended intensive care and long hospital stays for some patients with oesophageal cancer [8–10]. Inflammatory cytokines produced at the surgical site may play an important role in eliciting systemic inflammatory response and stress-induced organ dysfunction states are thought to be provoked by an uncontrolled inflammatory response due to the overproduction of these proinflammatory mediators [11]. Perioperative steroid therapy is reported to be effective for the improvement of the postoperative clinical course of patients with oesophageal cancer [12,13]. This is because steroids may attenuate surgical stress-induced inflammatory responses both directly by suppressing the release of proinflammatory cytokines and via inducing interleukin-10 synthesis [12,13]. We have already reported that a mechanism of pulmonary complications after oesophagectomy may be in part due to activation of polymorphonuclear leukocytes (PMN) by locally produced

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interleukin-8 [14]. Secretory leukocyte protease inhibitor (SLPI), a 12 kDa protein, is constitutively expressed in the lungs and potently inhibits PMN-derived protease activity [15–17] and we have already reported that SLPI in bronchoalveolar lavage fluid (BALF) was associated with the respiratory conditions after oesophagectomy [18]. Corticosteroids are reported to increase SLPI levels in airway epithelial cells and exert their anti-inflammatory effects [19–21], but there was no report showing whether perioperative steroid therapy really affected SLPI production in the lungs after oesophagectomy. Therefore, this study investigated the effect of a perioperative steroid therapy on the SLPI levels in the lungs and postoperative clinical course in patients who underwent oesophagectomy.

2. Materials and methods

2.1. Patients

Twenty-one consecutive patients who underwent radical oesophagectomy for oesophageal cancer at Gunma University Hospital in 2003–2004 were investigated in this study. All 21 patients were treated with perioperative steroid therapy {MP(+) group}. To make this study as objective and fair as possible, 15 consecutive patients operated on during a 1-year period in 2002, just before the start of the routine steroid therapy in 2003, were adopted as an historical control{MP(−) group}. In the MP(+) group, 250 mg of methylprednisolone was administered intravenously to each patient 1 h before the operation [12,13]. Thirty-two patients were male and four were female, and they were all Japanese. The average age was 61.1 ± 1.4. This protocol was approved by the university review board. Informed consent according to the Declaration of Helsinki was obtained from each of the patients enrolled in the study.

2.2. Clinical parameters

All patients had detailed preoperative risk assessment based on history, symptoms and signs of chronic lung or heart disease, chest X-ray, electrocardiogram, arterial blood gas analysis, pulmonary function tests and biochemical and haematological tests. Disturbance of organ function was investigated according to the criteria of Kuwano et al. [22]. Pathological classification of the primary tumour, the degree of lymphnode involvement and organ metastasis were examined according to the TNM/UICC classification [23].

2.3. Surgery and postoperative care

All patients underwent cervico-thoraco-abdominal three-field lymphnode dissection through a right thoracotomy [4,5]. At the end of the operation, all patients were admitted to the Intensive Care Unit, and placed on prophylactic mechanical ventilation. The timing of extubation was decided according to the criteria of Sato et al. [13] and Shimada et al. [12].

2.4. Definition of postoperative complications and systemic inflammatory response syndrome

The postoperative complications were defined as follows [12,13,21]. Pulmonary complications were defined by the presence of one or more of the following: (1) $paCO_2 > 50$ mmHg, (2) bilateral pulmonary infiltrates on a radiograph or (3) respiratory index >2.5. Anastomotic leakage was diagnosed by gastrography and clinical features. Liver dysfunction was defined by either the aspartate aminotransferase or alanine aminotransferase value being >200 IU/L. Arrhythmia was defined as the status requiring anti-arrhythmia drug therapy. Systemic inflammatory response syndrome (SIRS) was diagnosed when at least two of the following parameters appeared: body temperature (>38 °C or <36 °C), heart rate (>90 beats/min), tachypnea (>20 breaths/min), hyperventilation ($paCO_2$ <32 mmHg) and white blood cell count (>12,000 cells/mm^3 or <4000 cells/mm^3) [24].

2.5. BALF sampling and assay

BALF was obtained at the end of the surgery (postoperative day 0), on postoperative days 1–3 according to the method of Lee et al. [25]. Twenty-five millilitres of sterile 0.9% NaCl was instilled through a bronchofibre and aspirated by suction. The cells, debris and mucous were removed by centrifugation at 3000 rpm for 10 min. SLPI was measured by ELISA with an immunoassay kit (TECHNE Corporation, Minneapolis, MN, USA).

2.6. Statistical analysis

All data are presented as the mean ± S.E. Statistical significance was determined by Wilcoxon's rank test or chi-square test. A p-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Comparison of the groups

Patient characteristics and the degree of surgical stress in the two groups were compared (Table 1). The background of the groups was similar and statistical differences were not significant.

3.2. Effect of steroid therapy on postoperative morbidity and mortality

Postoperative mortality and morbidity in the groups were compared (Table 2). The mortality rate was 0%. There was no significant difference in the organ system or surgical complication rate between the two groups. The number of days until extubation and that of SIRS were more remark-