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ORIGINAL ARTICLE

Stress ulcer prophylaxis in patients being weaned from the ventilator in a respiratory care center: A randomized control trial

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lansoprazole OD;
proton pump inhibitor;
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stress ulcer prophylaxis;
weaning

Background/Purpose: No data has been available on prophylaxis for stress ulcer development during the process of weaning patients off mechanical ventilators. We conducted a randomized study to evaluate the efficacy of stress ulcer prophylaxis with lansoprazole OD in patients being weaned from mechanical ventilators.

Methods: A total of 120 patients were randomly allocated into two groups using blocked randomization, with 60 patients in each group. Group A was the treatment group, receiving lansoprazole OD 30 mg from a nasogastric tube for 14 days, while Group B, the control group, received no proton pump inhibitors or other medications for treating peptic ulcers. The primary end point of our study was apparent upper gastrointestinal bleeding within 2 weeks of enrollment.

Results: Apparent upper gastrointestinal bleeding occurred in zero patients and five patients in Groups A and B, respectively (Group A: 0% vs. Group B: 8.3%, $p = 0.057$). There was no significant difference between the two groups in ventilator-associated pneumonia (Group A: 6.7% vs. Group B: 10.0%, $p = 0.509$) and 30-day survival rates (Group A: 96.7% vs. Group B: 100%, $p = 0.496$).

Conclusion: Stress ulcer prophylaxis with lansoprazole in patients being weaned from mechanical ventilators led to a lower but not statistically significant incidence of apparent upper gastrointestinal bleeding. There was no significant increase of incidence of ventilator-

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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associated pneumonia in the prophylaxis group. Further larger scale studies are needed to clarify the benefit of stress ulcer prophylaxis in such patients.

Introduction

Stress ulcer prophylaxis (SUP) has been recommended for the prevention of upper gastrointestinal (UGI) bleeding and has become a standard of care in critical patients admitted to the intensive care unit (ICU).[1] Prolonged mechanical ventilation for >48 hours and coagulopathy were two independent risk factors for gastrointestinal bleeding.[2] Both histamine-2 receptor antagonists (H2RAs) and proton pump inhibitors (PPIs) are commonly used as antisecretory agents in the treatment of acid-related disease in clinical practice.[3,4] In previous studies, the H2RAs were the most common agents used in SUP.[5] In a recent meta-analysis, H2RAs offered no advantage for stress ulcer prophylaxis as compared to sucralfate in patients with mechanical ventilation, but had the disadvantage of higher rates of ventilator-associated pneumonia (VAP).[6] PPIs have been demonstrated to maintain better acid suppression than H2RAs[7] and have good prophylactic effects for stress ulcers.[8] In a cost-effectiveness analysis, PPI prophylaxis produced a more efficient prophylactic strategy for stress ulcer bleeding (SUB) than H2RAs.[9]

In clinical practice, the weaning program has sometimes been deferred due to UGI bleeding. During weaning from a mechanical ventilator, the weaning process will increase the oxygen cost of breathing[10] and generate a major energy demand to support the respiratory muscles.[11] As an organ, the gut is very sensitive to hypoxia.[12–14] Gastric mucosal acidosis and mucosal ischemia will develop when blood flow is diverted from the splanchnic vasculature to other tissues,[15,16] disturbing the defense mechanism of the gastric mucosa. Therefore, stress ulcers may occur as a manifestation of focal mucosal ischemia[17] during the weaning process.

SUP is commonly used in patients on a ventilator to prevent SUB.[18] However, no single strategy is preferred for SUP when mortality is used as the outcome in such patients.[5] In addition, medications for SUP in critically ill patients, including those on a ventilator, are not routinely recommended by the national insurance system in Taiwan. No data is currently available on the incidence of SUB and prophylaxis of stress ulcer development during the process of weaning patients from mechanical ventilators. Therefore, we conducted this study to investigate the efficacy of SUP and the incidence of VAP in patients being weaned from mechanical ventilators in a respiratory care center.

Patients and methods

Study design

This study was a prospective, randomized, non double-blind trial performed in a medical center, the Far Eastern Memorial Hospital, in New Taipei City, Taiwan. The study was designed in a respiratory care center using a weaning program for those difficult to wean patients in the medical or surgical ICUs. Patients who had received mechanical ventilation for >48 hours, had undergone nasogastric (NG) tube intubation, and were prepared to be weaned from the ventilator were included. Patients who were pregnant, <18 years old, allergic to lansoprazole, having active UGI bleeding, or receiving PPIs or H2RAs within 1 week were excluded. Surgical tracheostomy should be performed after 11–14 days of mechanical ventilation.[19] The study period was defined as 2 weeks. The mechanical ventilation settings of the patients fulfilling the criteria for weaning were as follows: SIMV (synchronized intermittent mandatory ventilation) plus PSV (pressure support ventilation) mode, respiration rate (f) ≤6/min, pressure support level ≤16 cmH_2O, and tidal volume ≥5 mL/kg.

Patients

From June 1, 2009 to February 29, 2012, 758 patients were admitted to the respiratory care center (RCC) due to difficulties being weaned off ventilators in the medical or surgical ICUs, and 534 patients were excluded due to recent use of PPIs, H2Ras, or death prior to enrollment. The definition of difficult weaning was patients who were not weaned off the mechanical ventilator 48–72 hours after the resolution of their underlying disease process. Among the 224 patients who started to be weaned and fulfilled the enrollment criteria, 104 patients were excluded because their families refused to sign the informed consent form. Finally, 120 patients were enrolled in this study (Fig. 1).

Study procedures

After obtaining written consent from their families, the patients were enrolled within 24 hours after beginning the weaning from the ventilator. They were randomly allocated into two groups using blocked randomization. Treatment Group A was given lansoprazole OD 30 mg once daily (takepron OD 30 mg/tab, TAKEDA Pharmaceutical Company, Ltd., Osaka, Japan) via NG tube for 14 days, while control Group B received no PPIs or other medications for treating peptic ulcers. We collected the following data: the use of ulcerogenic medications [such as, nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, steroids, and anticoagulants], comorbidities (including coronary artery disease, recent cerebrovascular accident, chronic obstructive pulmonary disease, diabetes mellitus, hypertension, heart failure, liver cirrhosis, uremia, and malignancy), histories of recent operations, peptic ulcer disease and UGI bleeding, initial APACHE II (Acute Physiology and Chronic Health Evaluation II) scores in the medical or surgical ICUs,