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Procalcitonin-guided antibiotic therapy in aspiration pneumonia and an assessment of the continuation of oral intake

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ABSTRACT

Background: Procalcitonin-guided antibiotic therapy for community-acquired pneumonia is effective and safe. However, the usefulness of procalcitonin for aspiration pneumonia and its nutrition-related outcomes are unknown.

Methods: We conducted a noninferiority randomized controlled study in patients with aspiration pneumonia who were admitted to our hospital between September 2010 and January 2012. We randomly assigned 105 patients to groups with different durations of antibiotic therapy based on the procalcitonin levels upon admission (procalcitonin group) or according to the standard guidelines (control group). The primary endpoints were relapse of aspiration pneumonia and death within 30 days, with a predefined noninferiority boundary of 10%. Secondary endpoints included duration of antibiotic exposure. Furthermore, we conducted a retrospective analysis of the prognostic factors that determined continuation of oral nutritional intake, relapse of pneumonia, and in-hospital death.

Results: The rate of relapse and death within 30 days were similar in the procalcitonin and control groups (25% versus 37.5%; difference, −12.5%; 95% confidence interval, −30.9% to 5.9%). Procalcitonin-guided antibiotic therapy significantly shortened the median duration of antibiotic exposure (5 versus 8 days; $p<0.0001$); however, the continuation of oral intake was not increased (56% versus 50%; $p=0.54$). A multivariable analysis showed a significant association between the continuation of oral nutritional intake and the body mass index upon admission.

Conclusions: Procalcitonin-guided antibiotic therapy for aspiration pneumonia can shorten the duration of antibiotic exposure, but it does not increase the continuation of oral intake (UMIN000004800).

Abbreviations: PCT, procalcitinin; NHCAP, nursing and healthcare-associated pneumonia; JRS, the Japan Respiratory Society; PEG, percutaneous endoscopic gastrostomy; CRP, C-reactive protein; CI, confidence interval; IQR, interquartile range; BMI, body mass index; A-DROP, age, dehydration, respiration, orientation, pressure; PNI, prognostic nutritional index; MWST, modified water-swallowing test

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1. Introduction

Aspiration pneumonia is a major cause of death among elderly or debilitated patients. Difficulty in swallowing (which may result from stroke, dementia, etc.) is not uncommon in this group of patients, and dysphagia with aspiration is considered the most important factor contributing to the risk of pneumonia in patients with stroke [1]. Aspiration is defined as the misdirection of oropharyngeal or gastric contents into the larynx and lower respiratory tract [2]. Among elderly patients, aspiration pneumonia often relapses and sometimes develops into refractory or fatal pneumonia because of repeated silent aspiration, which is a more important cause of pneumonia than the aspiration of gastric contents. Elderly people frequently receive poor oral care, which can lead to oropharyngeal colonization by potential respiratory tract pathogens, including *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*.

A nursing and healthcare-associated pneumonia (NHCAP) guideline has been proposed by the Japanese Respiratory Society (JRS) [3]. Patients with NHCAP are at an increased risk of developing antibiotic-resistant bacteria, especially after exposure to broad-spectrum antibiotics for >2 days during the previous 90 days or after receiving tube feedings [4]. In the treatment of aspiration pneumonia which is the major pathogenic mechanism of NHCAP, both decreasing antibiotic exposure and continuing oral nutritional intake are important for preventing the development of antibiotic-resistant bacteria.

To date, procalcitonin (PCT) has been used as a diagnostic marker of severe bacterial infection and sepsis. Measurement of the serum PCT concentration is useful for both the diagnosis of a bacterial infection and estimating the severity of systemic inflammatory reactions. If the PCT level is >0.5 ng/mL, there is always a suspicion of sepsis or a severe bacterial infection. In such cases, aggressive antibiotic use is recommended for patients with airway infections [5–7]. PCT-guided antibiotic therapy leads to an important reduction in antibiotic use in patients with lower respiratory tract infections without increasing the risk for serious adverse outcomes [5,7]. However, the usefulness of PCT-guided antibiotic use in patients with aspiration pneumonia is unclear.

We initiated a study to estimate the efficacy and safety of PCT-guided antibiotic therapy for decreasing antibiotic exposure in patients with aspiration pneumonia. Another aim of this study was to investigate whether PCT-guided antibiotic therapy contributes to the continuation of oral nutritional intake.

2. Methods

A prospective, randomized, open-label, noninferiority trial was conducted between September 2010 and January 2012. This study was approved by the institutional review board at our hospital (Approved date: July 20, 2010; Approved #: 8/2010) and registered at the university hospital medical information network (Registration date: December 27, 2010; Registration #: UMIN000004800). Eligible patients and their families provided written informed consent.

Patients at risk for aspiration, who had been hospitalized after developing pneumonia, were enrolled. Aspiration pneumonia was clinically diagnosed on the basis of the findings on computed tomography (CT) (for example, bronchopneumonia in the dorsal lower lobes), combined with a history of aspiration pneumonia, stroke or dementia, poor systemic condition, or any combination of these (for example, bedridden patients or patients fed by a nasogastric tube or percutaneous endoscopic gastrostomy [PEG]). We also referred to clinical symptoms such as choking or coughing while eating as suspected dysphagia [8]. Selection criteria included the following: at least 1 month had elapsed since the last treatment for relapsed pneumonia and ventilator use was not scheduled for the pneumonia treatment. Exclusion criteria included patients with a known severe allergy to any drugs; patients with sepsis or a severe infectious disease; patients with severe underlying diseases (for example, malignancy, chronic obstructive pulmonary disease [COPD], heart failure) that affected the prognosis; and patients who could not safely have cessation of oral intake or hydration as a treatment for aspiration pneumonia because of dementia.

Following enrollment, the patients were randomly allocated in a 1:1 ratio to groups assigned different durations of antibiotic therapy based on PCT levels upon admission (PCT group) or according to the standard guideline (control group). PCT levels were measured via outsourcing to SRL (Tokyo, Japan), and the results were obtained 2 or 3 days after admission. In the PCT group, if the PCT levels upon admission were <0.5 ng/mL, 0.5–1.0 ng/mL, or >1.0 ng/mL, the duration of antibiotic therapy was determined to be 3, 5, or 7 days, respectively [5]. If the PCT level upon admission was >5.0 ng/mL, we continued antibiotic treatment until it was less than 10% of the peak PCT level reached. In the control group, antibiotic therapy followed the recommendations of the JRS guideline for management of community-acquired pneumonia in adults [8]. Antibiotic therapy was discontinued if 3 of the following 4 criteria were met: fever declined (body temperature <37.0 °C), normalization of leukocyte count, decrease in the C-reactive protein (CRP) level to 30% of the maximum, and an obvious improvement as observed by chest radiography. In both groups, the choice of antibiotic regimen was left to the discretion of the treating physician.

The primary noninferiority endpoint was a composite of a relapse of aspiration pneumonia and death from any cause occurring within 30 days of admission. Predefined secondary endpoints were antibiotic exposure and adverse events from antibiotic therapy (the incidence of pseudomembranous enterocolitis). In this study, we assessed the fasting duration, length of hospital stay, and rate of the continuation of oral nutritional intake. Furthermore, we conducted a retrospective analysis of the prognostic factors that determined the continuation of oral nutritional intake, a relapse of pneumonia, and an in-hospital death, using multivariate logistic regression.

2.1. Statistical analysis

According to prior patient data from our hospital, the risk for a relapse of aspiration pneumonia and an in-hospital death was estimated to be 40%. As the efficacy of PCT-guided antibiotic therapy in patients with aspiration pneumonia was unclear, we estimated it to be 45%. As a tolerable upper limit, a noninferiority margin of 10% was chosen on the basis of guidelines issued by the Center for Drug Evaluation and Research and the Committee