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Bronchoscopic diagnosis of peripheral pulmonary lung cancer employing sedation with fentanyl and midazolam ☆

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ABSTRACT

Background: Sedation with fentanyl and midazolam during bronchoscopic examination is commonly employed by pulmonary physicians in the USA and Europe. We assessed the efficacy of such sedation in the bronchoscopic diagnosis of peripheral lung cancer.

Methods: We retrospectively evaluated data from 102 patients who underwent transbronchial biopsies (TBB) for diagnosis of peripheral lung cancer. Bronchoscopies with and without fentanyl were performed in 61 (group A) and 41 (group B) patients, respectively. Midazolam was administered to all patients. Medical records were retrieved, and between-group comparisons were made using unpaired Student's *t*-tests.

Results: The mean fentanyl dose was 49.5 μg (range: 10–100 μg), and midazolam doses in groups A and B were 4.29 mg (range: 1–14 mg) and 5.54 mg (range: 1–12 mg), respectively. Diagnostic histological specimens were obtained from 75.4% and 65.8% of group A and B patients, respectively ($P = 0.30$). The diagnostic sensitivities for lung cancer, via at least one of TBB, cytological brushing, or bronchial washing, in groups A and B were 88.5% and 70.4%, respectively ($P = 0.035$). Moreover, lesion diagnostic sensitivities, via at least one of TBB, cytological brushing, and bronchial washing, in groups A and B were 98.1% and 68.0%, respectively ($P = 0.01$).

Conclusion: Fentanyl and midazolam sedation during bronchoscopy facilitated the diagnosis of peripheral pulmonary lung cancers.

Abbreviations: BTS, British Thoracic Society; CT, computed tomography; EBUS, endobronchial ultrasound; TBB, transbronchial biopsy

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1. Introduction

The American College of Chest Physicians has recommended the use of a well-tolerated and synergistic benzodiazepine/opiate combination for sedation during bronchoscopy [1]. The British Thoracic Society (BTS) guidelines for diagnostic flexible bronchoscopy in adults also recommend using benzodiazepines and/or opiates [2]. We previously showed that sedation with fentanyl and midazolam was safe and useful during the bronchoscopic examination of Japanese patients [3]. Recent meta-analyses have indicated that new techniques, including endobronchial ultrasound (EBUS)-guided transbronchial biopsy (TBB) with placement of a guide sheath, navigation devices, and thin bronchoscopes, can improve the diagnostic yield of guided bronchoscopy by > 70% [4–6], but results are variable [7,8]. Furthermore, it is unclear whether sedation using fentanyl and midazolam during bronchoscopic examination improves the diagnostic sensitivity for lung cancer. Therefore, we investigated whether fentanyl and midazolam sedation facilitate the bronchoscopic diagnosis of lung cancer.

2. Materials and methods

2.1. Patients

We retrospectively reviewed patients who underwent bronchoscopy at the National Hospital Organization of the Okayama Medical Center, between November 2015 and December 2016. Bronchoscopy was performed in 102 consecutive patients with peripheral lung cancer. Since April 2016, fentanyl/midazolam sedation has been routinely used at our institution to aid in the diagnosis of peripheral lung cancer. All final diagnoses were based on TBB, cytological brushing, bronchial washing, EBUS-guided transbronchial needle aspiration, computed tomography (CT)-guided needle biopsy, and/or surgical resection. Fentanyl/midazolam sedation was employed in 61 patients, evaluated between April and December 2016 (group A). The historical control group was composed of 41 patients who underwent bronchoscopic examination after injection of midazolam only (without fentanyl), evaluated between November 2015 and March 2016 (group B). The diameters of the longest chest lesions on CT were recorded. The study was approved by the Institutional Ethics Committee of the National Hospital Organization, Okayama Medical Center on March 22, 2017 (approval no. H28-RINKEN-ZINSOKU-62).

2.2. Procedures

All patients underwent conventional flexible bronchoscopy (using BF-260, P260F, or P290 bronchovideoscopes; Olympus, Tokyo, Japan) and radial ultrasound probing (UM-S20-17S instrument, Olympus) employing a guide sheath kit (K-201, Olympus). Rapid on-site evaluation and navigation were performed (SYNAPSE VINCENT software; Fuji Film, Tokyo, Japan). The required numbers of TBBs were dictated by these evaluations; if malignant cells were pathologically evident on rapid on-site evaluation, no further biopsies were required and, conversely, if 10 biopsies failed to yield adequate tissue samples, no further biopsies were performed. We cytologically evaluated Papanicolaou-stained samples and histologically evaluated formalin-fixed paraffin-embedded samples stained with hematoxylin and eosin. Before each procedure, we injected 25 mg hydroxyzine pamoate and 50 mg guaifenesin intramuscularly, and sprayed 5 mL 2% (w/v) lidocaine into the pharynx. Additionally, 5 mL 2% (w/v) lidocaine were administered through the channel during each procedure. The bronchoscope was inserted orally under conscious sedation. When fentanyl is administered with other sedatives, an initial dose of 25–50 μg is recommended with additional doses of 25 μg, as required, until the desired effect is achieved. The recommended dose of midazolam is 0.01 – 0.1 mg/kg [3]. As Japanese are on an average physically smaller than Westerners, we selected a lower dose of fentanyl. Thus, in this study, fentanyl (20 μg) was administered intravenously to the patients just before the procedure, and fentanyl (10 μg) and midazolam (1 mg) were added as required [3]. Monitoring featured electrocardiography, pulse oximetry, and blood pressure measurements; no anesthesiologist was present.

2.3. Statistical analyses

Statistical analyses were performed using Microsoft Office Excel 2010 (Microsoft Japan Corporation, Tokyo, Japan). Between-group comparisons were made using unpaired Student's t-tests. The relationships between categorical variables were explored using chi-squared tests. P-values < 0.05 were considered statistically significant.

3. Results

Patients' characteristics and target lesions are shown in Table 1. The median lesion size was smaller in group A than B, however this difference was not statistically significant (29.0 mm vs. 29.3 mm; $P = 0.14$). The number of patients with nodules ≥ 20 mm in diameter was greater in group A than B ($n = 44$ vs. $n = 23$; $P = 0.01$). The incidence of squamous cell carcinoma was higher in group A than B ($n = 14$ vs. $n = 4$; $P = 0.018$). Among the 61 patients in group A, definitive diagnoses were achieved in 53 using bronchoscopy, 4 using CT-guided needle biopsy, 2 using surgical resection, and 2 using EBUS-guided transbronchial needle aspiration. Similarly, among the 41 patients in group B, definitive diagnoses were achieved in 29 using bronchoscopy, 9 using CT-guided needle biopsy, 2 using surgical resection, and 1 using analysis of pleural effusion. Group A patients received a mean fentanyl dose of 49.5 μg (range: 10 – 100 μg) and midazolam dose of 4.29 mg (range: 1 – 14 mg); group B patients received a mean midazolam dose of 5.54 mg (range: 1 – 12 mg).

The diagnostic sensitivity for lung cancer was higher in group A than B, using at least one of TBB, cytological brushing, or bronchial washing (88.5% vs. 70.4%; $P = 0.035$).

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