

Original Research

Investigation of antimicrobial therapy for aspiration pneumonia in elderly nursing homes: a retrospective observational study in Japan

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Abstract

Objective: Poor prognostic factors in the treatment of infectious diseases in home care have not been studied to date. Further, there have been no studies on the appropriate use of antimicrobial agents for aspiration pneumonia in elderly nursing home. Therefore, this study was retrospectively investigated the status of antimicrobial use for aspiration pneumonia in elderly nursing homes, and the clinical efficacy of each antimicrobial therapy. **Methods:** Patients who received antimicrobial therapy for aspiration pneumonia between 2020 and 2022 were included. This study was investigated the compliance of antimicrobial therapy with recommended Japanese guidelines. The clinical efficacy and safety of the recommended and non-recommended antimicrobial therapies were examined. **Results:** Fifty patients with aspiration pneumonia were administered antimicrobials. The rate of compliance to the guidelines for the appropriate selection, dose, and duration of antimicrobials were 46%, 66%, and 66%. This investigation indicated that all three indicators were appropriate showed a higher clinical cure rate and lower mortality rate than those in groups for which all three indicators were inadequate (clinical cure, 91.7% vs. 0%, $p = 0.008$; 30-days mortality, 8.3% vs. 33.3%, $p = 0.371$). In addition, appropriate drug selection resulted in lower mortality, and appropriate dosing duration was significantly associated with better clinical cure rates ($p < 0.0001$). **Conclusions:** Overall, the appropriate use of antimicrobials according to the guidelines appears to be associated with improved clinical outcomes in the treatment of aspiration pneumonia in elderly nursing homes.

Keywords: aspiration pneumonia; elderly nursing home; practice guidelines; Japan

INTRODUCTION

Community-acquired pneumonia (CAP) is a common disease that causes high mortality and long hospitalization periods in the elderly population.¹ Aspiration pneumonia is estimated to account for 5–15% of CAP cases.² The mortality rate of aspiration pneumonia is gradually increasing worldwide and is reported to be 21%.³ Thus, the establishment of appropriate antimicrobial therapy for aspiration pneumonia is an immediate priority to prevent severe bacterial infections in the elderly population.

Currently, inappropriate use of antimicrobials and the consequent development of resistant strains has become a global problem.⁴ In Japan, the inappropriate use of antimicrobials is primarily via the oral route (93%), with most

prescriptions in outpatient settings.^{5,6}

Considering the social background of an aging society and an increase in the number of patients with chronic diseases, home medical care is being increasingly promoted with the goal of enabling patients to live with their illnesses. However, in the treatment of acute diseases, such as infectious diseases, home healthcare tends to have a higher risk of treatment difficulties than inpatient care due to delay in noticing the worsening of symptoms. However, to date, there are no surveys or studies on the actual status and appropriate use of antimicrobials in home care including elderly nursing homes in the community. Moreover, the appropriate use of antimicrobial therapy for aspiration pneumonia in elderly nursing homes is not mentioned in any current guidelines. In fact, aspiration pneumonia in the elderly is treated at home empirically by individual physicians.

In this study, we retrospectively investigated the current situation of antimicrobial therapy in elderly nursing homes and evaluated its effectiveness and safety in elderly patients with aspiration pneumonia.

METHODS

Patient population

We retrospectively reviewed the medical records of patients who received antimicrobial therapy for aspiration pneumonia at a nursing home (capacity of 27 residents; Mie, Japan) from May 2020 to June 2022. The following patients were excluded from the study: (1) patients less than 64 years old and (2)

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patients who received antimicrobials for less than 2 days (Figure 1). According to previously published international guidelines, pneumonia is diagnosed by a constellation of clinical features and a demonstrable infiltrate on chest radiography or other imaging techniques.^{7,8} Aspiration pneumonia is defined as pneumonia among patients who have at least one of several aspiration-related risk factors, including episodes of aspiration, dysphagia, disturbance of consciousness, neuromuscular diseases, cerebrovascular diseases, tube feeding, or bedridden status.⁹ Aspiration pneumonia was diagnosed by a physician based on the diagnostic criteria for aspiration pneumonia. The severity of pneumonia was assessed using the quick Sequential Organ Failure Assessment (qSOFA) score and A-DROP, and the treatment strategy was determined considering the severity and risk of bacterial resistance in routine practice.^{10,11} This study was reviewed and approved by the Ethics Committee of Mie University Hospital (No. H2022-128).

Data collection

Treatment data, including demographics, comorbidities, swallowing function, nutritional status, cognitive function, physical function, concomitant medications and laboratory data were retrospectively collected from medical records. Clinical outcomes and adverse events related to antimicrobial therapy were recorded for each patient.

Compliance of guidelines

According to the Japanese Respiratory Society (JRS) guidelines

for the management of pneumonia in adults, the treatment strategy for empiric treatment of aspiration pneumonia was determined by the severity of illness and the risk of resistant organisms.¹² For patients with non-severe infections and a low risk of bacterial resistance, narrow-spectrum antibacterial agents, such as respiratory quinolones, amoxicillin/clavulanate, and ceftriaxone, were recommended. Ceftriaxone, sulbactam–ampicillin, and injectable levofloxacin were recommended for patients with severe infection and a low risk of bacterial resistance. For patients with severe infection and a high risk of bacterial resistance, tazobactam/piperacillin, fourth-generation cepheems, carbapenems, and quinolones with antimicrobial activity against *Pseudomonas aeruginosa* were recommended. The JRS guidelines recommend 5–7 days of antimicrobial therapy for aspiration pneumonia. Drug selection, dose, and duration were defined as appropriate when they were used in accordance with JRS guidelines above mentioned. In addition, the risk classification of resistant bacteria was evaluated by two researchers (YN and HK).

Data analysis

First, we investigated the actual use of antimicrobials, including their usage, effectiveness, and safety. Second, we evaluated the appropriateness of antimicrobials for selection, dose, and dosing duration based on the JRS guidelines. Finally, we compared effectiveness and safety between patients receiving appropriate and inappropriate antimicrobial therapy in terms of selection, dose, and duration of antimicrobial therapy.

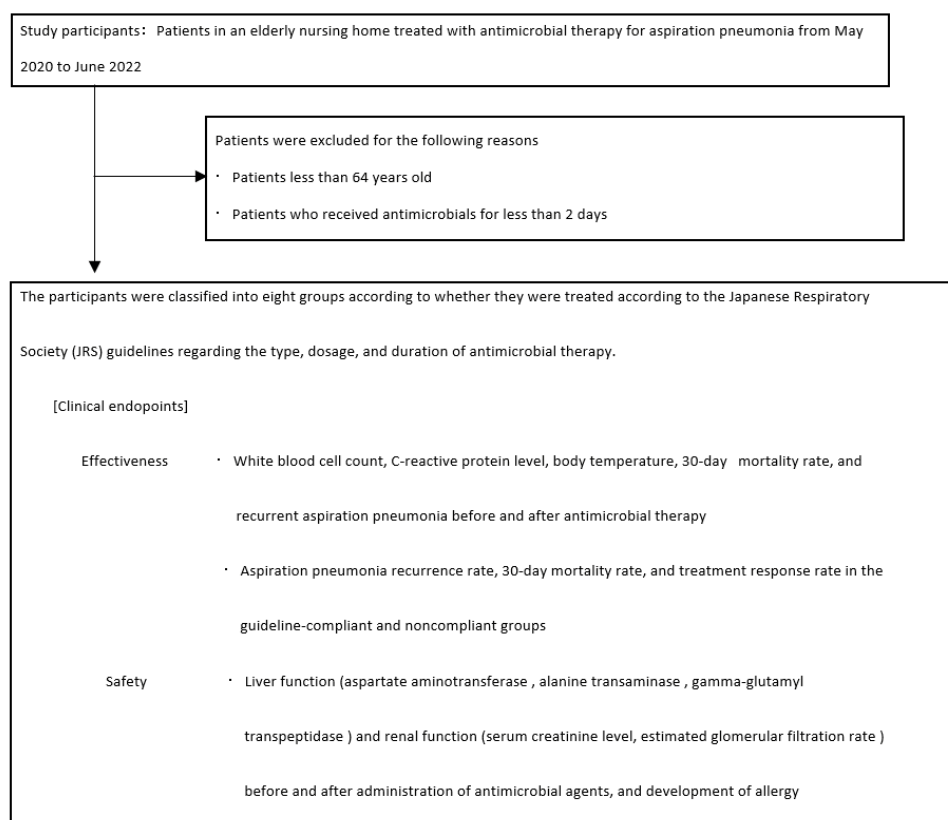


Figure 1. Participant disposition for study



Furthermore, similar comparisons were performed in the following subgroups: group 1, patients in whom antimicrobial therapy was appropriate in all the three parameters (selection, dose, and duration); group 2, patients in whom antimicrobial therapy was inappropriate in all the three parameters; group 3, patients in whom antimicrobial therapy was administered with appropriate selection and dose; group 4, patients in whom antimicrobial therapy was appropriate regarding selection and duration; group 5, patients in whom antimicrobial therapy was appropriate regarding dose and duration; group 6, patients in whom antimicrobial therapy was appropriate only in drug selection; group 7, patients in whom antimicrobial therapy was given only in appropriate dose; group 8, patients in whom antimicrobial therapy was given only in appropriate duration.

Clinical effectiveness

Clinical responses to antimicrobial therapy were classified as clinical cure, clinical improvement, and treatment failure, each of which was judged by one physician and one pharmacist at the end of antimicrobial administration.¹³ Clinical cure was defined as the resolution of clinical signs and symptoms of baseline pneumonia and the completion of antimicrobial therapy within 7 days. Clinical improvement was defined as the absence of a clinical cure, but improvements in baseline signs and symptoms of pneumonia at the end of antimicrobial therapy. Treatment failure was defined as the persistence or progression of baseline signs and symptoms of pneumonia and/or the administration of other effective antimicrobials. Data regarding inflammation markers, such as white blood cell (WBC) count, C-reactive protein (CRP), and body temperature, were collected within 3 days before initiation of antimicrobial therapy and 3 days after the end of antimicrobial therapy. We also evaluated the recurrence rates of aspiration pneumonia and the 30-day mortality rates. Recurrence of aspiration pneumonia was defined as recurrence within 30 days after the end of antimicrobial therapy. The 30-day mortality was defined as death within 30 days after the initiation of antimicrobial therapy.

Safety evaluation

Abnormal laboratory data were evaluated using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Abnormalities were defined as follows: aspartate aminotransferase (AST): ≥ 3 times upper limit of normal; alanine transaminase (ALT): ≥ 3 times upper limit of normal; gamma-glutamyl transpeptidase (γ -GTP): ≥ 2.5 times upper limit of normal; serum creatinine (SCr): ≥ 1.5 times upper limit of normal; estimated glomerular filtration rate (eGFR): < 59 ml/min/1.73. We also assessed the development of allergies to antimicrobials.

Statistical analysis

Data regarding the clinical characteristics of patients were expressed as median values (minimum-maximum). Statistical significance was evaluated using the chi-square test for categorical data and unpaired t-test for continuous data. Statistical analyses were performed using JMP software, version 10.0 (SAS, Tokyo, Japan). A p value of < 0.05 was required to

achieve statistical significance.

RESULTS

Patients

Fifty patients met the inclusion criteria and were included in the study. Table 1 shows the demographic and clinical characteristics of the antimicrobials. The overall median age was 89 years and median nursing care level of the Ministry of Health, Labour and Welfare (Japan) was five.¹⁴ All included patients had mild aspiration pneumonia with a qSOFA score of one. Of the included patients, 70% had an A-DROP score of 0–1, and 28% had a score of two.

Trends in antimicrobial therapy and testing

Six types of antimicrobials were administered as shown in Table 1. The demographic and clinical characteristics did not differ significantly among the groups (Table 1). Body temperature, WBC count and CRP level were measured in 64% of the patients before and 24% of the patients after antimicrobial administration. Microbial testing was conducted in 24% of the patients before antimicrobial therapy, whereas sputum culture was not performed for any patient after antimicrobial therapy. Of all the included patients, 56.0% had a recurrence of aspiration pneumonia and 16.0% died. Moreover, the percent changes in body temperature, WBC count, and CRP level were 96.1%, 64.3%, and 39.1%, respectively (Table 2). Patients receiving macrolides and quinolones had comparable mortality rates (macrolides, 10.0%; quinolones, 14.3%), whereas patients treated with quinolones had a lower recurrence rate of aspiration pneumonia than those treated with macrolides (Table 2). Hepatic and renal impairments were observed in two patients and one patient, respectively. One patient who received quinolone showed an increase in AST and ALT levels, and one patient who received β -lactam/ β -lactamase inhibitor showed an increase in γ -GTP levels. The levels of SCr and eGFR increased in one patient receiving quinolone. However, no adverse events leading to discontinuation of treatment were observed.

Overall appropriateness of antimicrobial therapy

The selection of antimicrobials was appropriate in 46% of all the patients, including 65.4% of patients treated with β -lactam/ β -lactamase inhibitors and 85.7% of patients treated with quinolones. An appropriate dose was administered to 66% of all the patients, including 50% of patients receiving β -lactam/ β -lactamase inhibitors and in 100% of patients receiving macrolides, quinolones, and tetracyclines. The proportion of patients treated with appropriate duration was 66%. All patients who were treated with an inappropriate duration received antimicrobials for more than 10 days (Table 3).

Clinical effectiveness of appropriate use in the three indicators

Patients treated with antimicrobials recommended by the JRS Guidelines had improved clinical response, mortality, and recurrent aspiration pneumonia compared with patients receiving antimicrobials not recommended by the JRS



	Antibiotics (number)							
Characteristics	β -lactam/ β -lactamase inhibitor (26)	Macrolides (10)	Quinolone (7)	Tetracycline (3)	Cephalosporin (3)	Aminoglycosides (1)	p value	Overall
Gender (male/female)	26 (12/14)	10 (4/6)	6 (1/6)	3 (2/1)	3 (1/2)	1 (0/1)	0.587	50 (20/30)
Age (years)	89 (67–93)	88.5 (67–92)	88.5 (81–93)	88 (87–91)	85 (74–89)	91	0.721	89 (67–93)
Nursing care level	5 (3–5)	5 (4–5)	5 (4–5)	4 (4–5)	5 (3–5)	5	0.422	5 (3–5)
Serum creatinine (mg/dL)	0.50 (0.34–0.90)	0.54 (0.47–0.84)	0.47 (0.38–0.87)	0.55 (0.46–0.61)	0.68 (0.5–0.87)	0.43	0.812	0.50 (0.34–0.90)
eGFR (mL/min/1.73m ²)	85.7 (58.1–159.8)	84.9 (53.4–118.7)	90.0 (46.7–112.9)	103.2 (67.7–125.9)	84.1 (46.7–86.0)	98.9	0.662	85.7 (46.7–159.8)
qSOFA $\geq$ 2 (n,%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0–0)	0 (0)	–	0 (0)
A-DROP	1 (0–3)	1 (0–2)	1 (1–2)	1 (1–2)	1 (1–1)	2	0.566	
0–1	16 (61.5)	8 (80.0)	6 (85.7)	2 (66.7)	3 (100)	0 (0)		35 (70.0)
2	9 (34.6)	2 (20.0)	1 (14.3)	1 (33.3)	0 (0)	1 (100)		14 (28.0)
3	1 (3.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		1 (2.0)
4–5	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		0 (0)
Antimicrobial dose (mg/day)	SBT/ABPC(9) 3 (g/day) AMPC/CVA(17) 750	200	LVFX(6) 500 JAN(1) 75	100	300	100	–	–
Duration of antimicrobials (day)	7 (4–63)	8.5 (5–10)	7 (5–10)	7 (5–11)	5 (5–7)	5	0.992	7 (4–63)
Cerebrovascular disease(n,%)	8 (30.8)	2 (20.0)	1 (14.3)	1 (33.3)	1 (33.3)	0 (0)	0.924	13 (26.0)
Dementia(n,%)	23 (88.5)	8 (80.0)	7 (100)	1 (33.3)	3 (100)	1 (100)	0.668	44 (88.0)
Neuromuscular disease(n,%)	19 (73.1)	7 (70.0)	7 (100)	1 (33.3)	2 (66.7)	1 (100)	0.372	36 (72.0)
Respiratory disease (n,%)	6 (23.1)	2 (20.0)	0 (0)	1 (33.3)	0 (0)	0 (0)	0.672	9 (18.0)
Gastroesophageal disease (n,%)	11 (42.3)	4 (40.0)	0 (0)	0 (0)	0 (0)	1 (100)	0.077	16 (32.0)
Hypertension(n,%)	14 (53.8)	5 (50.0)	4 (57.1)	2 (66.7)	1 (33.3)	1 (100)	0.909	26 (52.0)
Diabetes mellitus (n,%)	0 (0)	0 (0)	1 (14.3)	0 (0)	1 (33.3)	0 (0)	0.062	2 (4.0)
Heart disease(n,%)	7 (26.9)	2 (20.0)	0 (0)	0 (0)	1 (33.3)	0 (0)	0.600	10 (20.0)
COPD (n,%)	3 (11.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.736	8 (16.0)
Japan Coma Scale	1 (0–3)	1 (1–2)	1 (0–2)	1 (1–2)	1 (1–2)	1	0.722	1 (0–2)
Urethral catheter placement(n,%)	11 (42.3)	5 (50.0)	0 (0)	0 (0)	1 (33.3)	1 (100)	0.121	18 (36.0)
Oral intake(n,%)	10 (38.5)	3 (30.0)	2 (28.6)	0 (0)	2 (66.7)	0 (0)	0.597	17 (34.0)
Assistance with eating(n,%)	9 (34.6)	3 (30.0)	1 (14.3)	0 (0)	1 (33.3)	0 (0)	0.753	15 (30.0)
Sputum suction (n,%)	21 (80.8)	7 (70.0)	5 (71.4)	3 (100)	1 (33.3)	1 (100)	0.460	38 (76.0)
PEG creation (n,%)	11 (42.3)	4 (40.0)	1 (14.3)	2 (66.7)	0 (0)	1 (100)	0.283	19 (38.0)
Enteral nutrition (n,%)	18 (69.2)	7 (70.0)	5 (71.4)	3 (100)	1 (33.3)	1 (100)	0.631	34 (68.0)
Dysphagia (n,%)	25 (96.2)	10 (100)	7 (100)	3 (100)	2 (66.6)	1 (100)	0.186	47 (94.0)
Dysphagia Severity Scale	4 (2–7)	4 (2–5)	4 (4–5)	4 (4–4)	5 (4–7)	4	0.235	4 (2–7)

Body Mass Index(kg/m ²)	19.9 (15.0–23.3)	19.9 (17–20.6)	15.4	N.D.	N.D.	19.9	0.232	19.9 (15.0–23.3)
Albumin(g/dL)	3.0 (1.9–4.1)	3.1 (2.5–3.6)	3.25 (3.1–3.6)	3.1 (2.5–3.3)	3.3 (3.2–4.1)	2.9	0.377	3.1 (1.9–4.1)
The independence level of daily life for elderly people with dementia	4 (3–4)	4 (3–4)	4 (3–4)	4 (4–4)	4 (3–4)	4	0.870	4 (3–4)
HDS-R	0 (0–2)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–2)	0	0.186	0 (0–2)
Activities of Daily Living	3 (2–3)	3 (2–3)	3 (2–4)	3 (3–3)	2 (0–3)	3	0.740	3 (3–4)
Number of drugs taken	5.5 (2–9)	6 (3–8)	4 (1–8)	6 (4–6)	5 (4–8)	5	0.806	5 (1–9)
ACE inhibitor (n,%)	10 (38.5)	3 (30.0)	0 (0)	1 (33.3)	0 (0)	1 (100)	0.191	15 (30.0)
Inhaled corticosteroid (n,%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	–	0
Antipsychotic (n,%)	3 (11.5)	0 (0)	1 (14.3)	0 (0)	0 (0)	0 (0)	0.641	5 (10.0)
Anxiolytic (n,%)	1 (3.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.972	1 (2.0)
Anticholinergics (n,%)	2 (7.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.878	2 (4.0)
Hypnotic (n,%)	2 (7.7)	0 (0)	1 (14.3)	0 (0)	0 (0)	0 (0)	0.859	3 (6.0)
Anticonvulsant (n,%)	1 (3.8)	0 (0)	1 (14.3)	0 (0)	1 (33.3)	0 (0)	0.332	3 (60)
Antidepressants (n,%)	1 (3.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.972	1 (2.0)

Kruskal–Wallis test for categorical data and Scheffé's test for continuous data; $p < 0.05$. Continuous data are shown as median (minimum–maximum).

SBT/ABPC, sulbactam/ampicillin; AMPC/CVA, amoxicillin/clavulanate; LVFX, levofloxacin; JAN, lasculofloxacin hydrochloride.

eGFR, estimated glomerular filtration rate; qSOFA, quick Sequential Organ Failure Assessment; A-DROP, Japan Respiratory Society community-associated pneumonia severity index; COPD, chronic obstructive pulmonary disease; PEG, percutaneous endoscopic gastrostomy; HDS-R, Hasegawa Dementia Scale-Revised.

Table 2. Clinical efficacy of antimicrobial agents					
	Percentage changes in the parameters			Recurrent aspiration pneumonia (n,%)	30-day mortality (n,%)
	Body temperature (%)	WBC (%)	CRP (%)		
Overall (n=50)	96.1 (91.0–99.7)	64.3 (32.5–147.8)	39.1 (0.4–200)	28 (56.0%)	8 (16.0%)
β-lactam/β-lactamase inhibitor (n=26)	96.1 (91.0–98.7)	64.3 (32.5–101.1)	32.1 (0.4–200.0)	11 (42.3%)	6 (23.1%)
Macrolides (n=10)	97.5 (94.8–99.2)	NA	NA	9 (90.0%)	1 (10%)
Quinolone (n=7)	97.1 (93.4–99.7)	64.6	91.7	1 (14.3%)	1 (14.3%)
Tetracycline (n=3)	96.1 (93.9–96.3)	86.5 (53.1–100)	87.8 (24.1–99.4)	1 (33.3%)	1 (33.3%)
Cephalosporin (n=3)	97.1 (95.6–98.4)	147.8	17.6	2 (66.6%)	0 (0%)
Aminoglycosides (n=1)	97.4	NA	NA	1 (100%)	0 (0%)

Percentage changes in temperature, WBC, and CRP levels before and after antimicrobial administration. Continuous data are shown as median (minimum–maximum). NA; Not Available; WBC, white blood cells; CRP, C-reactive protein.

Table 3. Appropriateness of antibiotics use assessed using the three parameters		
	Appropriately used / Frequency (n,%)	Inappropriately used / Frequency (n,%)
Right antimicrobials	23 (46.0)	27 (54.0)
β-lactam/β-lactamase inhibitor (n=26)	17 (65.4)	9 (34.6)
Macrolides (n=10)	0 (0)	10 (100)
Quinolone (n=7)	6 (85.7)	1 (14.3)
Tetracycline (n=3)	0 (0)	3 (100)
Cephalosporin (n=3)	0 (0)	3 (100)
Aminoglycosides (n=1)	0 (0)	1 (100)
Right dose	33 (66.0)	17 (34.0)



β-lactam/β-lactamase inhibitor (n=20)	13 (50.0)	13 (50.0)
Macrolides (n=10)	10 (100)	0 (0)
Quinolone (n=7)	7 (100)	0 (0)
Tetracycline (n=3)	3 (100)	0 (0)
Cephalosporin (n=3)	0 (0)	3 (100)
Aminoglycosides (n=1)	0 (0)	1 (100)
Right duration	33 (66.0)	17 (34.0)
β-lactam/β-lactamase inhibitor (n=20)	18 (69.2)	8 (30.8)
Macrolides (n=10)	5 (50.0)	5 (50.0)
Quinolone (n=7)	5 (71.4)	2 (28.4)
Tetracycline (n=3)	2 (66.6)	1 (33.3)
Cephalosporin (n=3)	2 (66.6)	1 (33.3)
Aminoglycosides (n=1)	1 (100)	0 (0)

Table 4. Comparison of clinical efficacy between recommended and non-recommended antimicrobial groups

	Right antimicrobials (n=23)	Wrong antimicrobials (n=27)	p value	Right dose (n=33)	Wrong dose (n=17)	p value	Right duration (n=33)	Wrong duration (n=17)	p value
A-DROP	1 (0–2)	1 (0–3)	–	1 (0–3)	1 (1–2)	–	1 (0–3)	1 (0–2)	–
Body temperature (%)	96.1 (93.4–99.7)	96.6 (91.0–99.2)	0.167	96.6 (91.0–106.4)	96.1 (94.6–97.4)	0.038	96.6 (93.8–99.7)	96.1 (91.0–100.0)	0.311
WBC (%)	60.6 (32.5–81.4)	90.7 (53.1–147.8)	0.833	68.3 (48.4–147.8)	60.9 (32.5–101.1)	0.279	64.6 (32.5–100.0)	88.6 (53.8–147.8)	0.006
CRP (%)	29.8 (0.4–200)	48.6 (13.9–99.4)	0.255	25.1 (0.4–200)	42.1 (10.9–96.7)	0.384	39.1 (0.4–200)	36.9 (13.0–99.4)	0.246
Recurrent aspiration pneumonia (n, %)	11 (47.8%)	17 (63.0%)	0.418	18 (54.5%)	10 (58.9%)	0.772	16 (51.6%)	12 (70.1%)	0.135
30-day mortality (n, %)	3 (13.0%)	6 (22.2%)	0.399	6 (18.2%)	3 (17.6%)	0.962	6 (18.2%)	3 (17.6%)	0.962
Clinical response									
Clinical cure	16 (70.0%)	12 (44.4%)	0.074	21 (63.6%)	7 (41.2%)	0.129	25 (75.8%)	2 (11.7%)	<0.0001
Clinical failure	7 (30.4%)	15 (55.6%)		12 (36.4%)	10 (58.8%)		8 (24.2%)	15 (88.2%)	

Chi-square test for categorical data and unpaired t-test for continuous data, $p < 0.05$. Continuous data are shown as median (minimum-maximum). Percentage changes in temperature, WBC, and CRP levels before and after antimicrobial administration. Data are shown as median (minimum-maximum). A-DROP, Japan Respiratory Society community-associated pneumonia severity index; WBC, white blood cells; CRP, C-reactive protein.

Guidelines, while there was no significant difference (Table 4). Patients treated with the right dose of antimicrobials had significantly decreased body temperature (96.6% [91.0–106.4%] vs. 96.1% [94.6–97.4%], $p = 0.038$) and a tendency to improve clinical response (63.6% vs. 41.2%, $p = 0.129$) compared to those treated with the wrong dose (Table 4). Patients treated for the right duration had significantly decreased WBC

and improved clinical response WBC, 64.6% [32.5–100.0%] vs. 88.6% [53.8–147.8%], $p = 0.006$; clinical response, 75.8% vs. 11.7%, $p < 0.001$) than those treated for the wrong duration (Table 4).

Safety evaluation with appropriate use in the three indicators

Several patients had abnormal laboratory data; abnormalities



in AST and ALT, γ -GTP, and SCr and eGFR were observed in one patient each. For patients with hepatic dysfunction, antimicrobial selection, dose and dosing duration were all appropriate. For patients with renal dysfunction, dose, and dosing duration were appropriate, however antimicrobial selection were not appropriate.

Clinical effectiveness in each group

Table 5 shows the clinical efficacy in each group. Twelve patients were treated with the appropriate amount of all three parameters (selection of antimicrobial agent, dose, and duration) (Group 1), while three patients were treated with all three indicators in inappropriate amounts (Group 2). Patients in group 1 showed a higher clinical cure rate and lower mortality rate than those in group 2 (clinical cure, 91.7% vs. 0%; 30-days mortality, 8.3% vs. 33.3%). In contrast, the rate of recurrent aspiration pneumonia in group 1 was comparable to that in group 2 (33.3% vs. 33.3%). Compared to the group 1, the groups that selected inappropriate antimicrobials or doses (groups 4 and 5) showed an increase in the clinical failure rate, recurrence rate of aspiration pneumonia, and mortality (group 1 vs. group 4 vs. group 5: clinical failure, 8.3% vs. 66.7% vs. 25.0%; recurrent rate, 33.3% vs. 66.7% vs. 58.3%; mortality, 8.3% vs. 33.3% vs. 25.0%). Next, the groups in which one of the three indicators (groups 6, 7, and 8) was appropriate were compared to group 2. Although the recurrence rate of aspiration pneumonia was higher in groups 6 (right drug selection) and 8 (right duration) than in group 2 (group 2 vs. group 6 vs. group 7, 33.3% vs. 75.0% vs. 77.8%), groups 6 and 7 (right dose) showed improved clinical failure and mortality rates compared to group 2 (group 2 vs. group 6 vs. group 7: clinical failure, 100% vs. 50.0% vs. 100%; mortality, 33.3% vs. 0% vs. 22.2%). The clinical outcomes in group 8 were comparable to those in group 1 (group 1 vs. group 8: clinical failure, 8.7% vs. 0%; recurrent rate, 33.3% vs. 66.7%; mortality, 8.3% vs. 0%) (Table 5).

DISCUSSION

Appropriate use of antimicrobials in elderly nursing homes

remains a challenge due to antimicrobial resistance.^{15,16} Previous studies have shown that antimicrobials are prescribed more inappropriately, more frequently, and for longer periods of time in elderly nursing homes than in inpatient or outpatient settings.¹⁷⁻²¹ The causative organisms of CAP are generally anaerobic bacteria and streptococci in the oral cavity.²² Macrolides have no spectrum against anaerobic bacteria, and macrolide resistance in streptococci has been frequently observed in Japan.²³ Therefore, macrolides should be inappropriate as an empirical antibiotic for patients with CAP in elderly nursing rooms.

In this study, we investigated the use, efficacy, and safety of antimicrobials for aspiration pneumonia in elderly nursing homes. Antimicrobial administration was performed through empirical therapy, and 24% of the included patients adhered to the JRS guidelines. The treatments following the JRS guidelines for drug selection, dose, and dosing duration was significantly superior to the non-compliant group in terms of clinical outcomes. Therefore, adherence to the JRS guidelines for empiric therapy can contribute to improved efficacy in the treatment of aspiration pneumonia in the elderly. The JRS guidelines are also recommended bacteriological tests to ensure appropriate antimicrobial therapy for patients in elderly nursing homes, however, 76% of patients did not undergo bacteriological tests prior to antimicrobial administration.

Our study shows that compliance with the JRS guidelines was 46%, 66%, and 66% for drug selection, dose, and dosing duration, respectively. Overall, 24% of eligible patients adhered to the JRS guidelines. In a study at a Japanese general hospital, among 84 nursing and healthcare-associated pneumonia (NHCAP) patients, 31 were in the treatment group that followed the JRS guidelines while 53 were in the non-adherence group, indicating a compliance rate of 36.9%.²⁴ A study evaluating the appropriate use of antimicrobials in the United States (U.S.) reported that 20.5% of CAP patients were prescribed appropriate antimicrobials.²⁵ Additionally, it has been reported that 6.9% of patients with CAP in the U.S. received treatment for the recommended duration.²⁶ Most studies have reported that

	Group 1 (n=12)	Group 2 (n=3)	Group 3 (n=1)	Group 4 (n=6)	Group 5 (n=12)	Group 6 (n=4)	Group 7 (n=9)	Group 8 (n=3)
A-DROP	1 (0-2)	1 (1-2)	1	1 (1-2)	1 (1-3)	1 (1-2)	1 (0-2)	1 (1-2)
Clinical response								
Clinical cure	11 (91.7%)	0 (0%)	0 (0%)	2 (33.3%)	9 (75.0%)	2 (50.0%)	0 (0%)	3 (100%)
Clinical failure	1 (8.3%)	3 (100%)	1 (100%)	4 (66.7%)	3 (25.0%)	2 (50.0%)	9 (100%)	0 (0%)
Recurrent aspiration pneumonia (n, %)	4 (33.3%)	1 (33.3%)	0 (0%)	4 (66.7%)	7 (58.3%)	3 (75.0%)	7 (77.8%)	2 (66.7%)
30-day mortality (n, %)	1 (8.3%)	1 (33.3%)	0 (0%)	2 (33.3%)	3 (25.0%)	0 (0%)	2 (22.2%)	0 (0%)

A-DROP, Japan Respiratory Society community-associated pneumonia severity index. Continuous data are shown as median (minimum-maximum).

Group 1: Right antimicrobials, right dose, and right duration; Group 2: Wrong antimicrobials, wrong dose, and wrong duration; Group 3: Right antimicrobials, right dose, and wrong duration; Group 4: Right antimicrobials, wrong dose, and right duration; Group 5: Wrong antimicrobials, right dose, and right duration; Group 6: Right antimicrobials, wrong dose, and wrong duration; Group 7: Wrong antimicrobials, right dose, and wrong duration; Group 8: Wrong antimicrobials, wrong dose, and right duration.



compliance with international antimicrobial guidelines for CAP is associated with the improvement of clinical outcomes.²⁷⁻²⁹ Moreover, it has been reported that compliance with nursing and healthcare-associated pneumonia guidelines does not worsen mortality, duration of antibiotic therapy and length of hospital stay.²⁴ These results are consistent with our findings.

A comparison of the effectiveness of antimicrobial selection showed that the recommended group had a higher rate of clinical cure than the non-recommended group. The inappropriate selection of antimicrobials has been reported to associate with a high rate of poor patient outcomes such as reoperation, rehospitalization, additional administration of different antimicrobials, longer hospital stays and treatment, high mortality, and increased treatment costs.³⁰⁻³² Our results suggest that the appropriate selection of antimicrobials may improve the effectiveness of treatment of aspiration pneumonia in ambulatory care, especially in elderly nursing homes.

The principle of antimicrobial therapy is to administer an appropriate dose of antimicrobials, regardless of the severity of pneumonia. The appropriate dose improved clinical efficacy; however, it did not significantly enhance clinical efficacy, suggesting that appropriate dose alone is not a sufficient condition. Therefore, other indicators, such as the selection of antimicrobials and the dosing duration, may also be critical factors in improving clinical efficacy. It has been shown that short-term antimicrobial chemotherapy of 5 to 7 days is sufficient in patients with CAP.^{33,34} In the case of ventilator-associated pneumonia, American guidelines recommend 7 days of antimicrobial therapy.³⁵ However, the duration of antimicrobial therapy for NHCAP has not yet been adequately investigated. Our study showed that most patients completed antimicrobial therapy within 5–7 days. Although 17 patients continued antimicrobial therapy for ≥ 10 days, only two patients died. These patients were monitored for WBC counts and CRP levels during treatment and showed decreases in both levels. Therefore, monitoring the WBC count and CRP level should be important in deciding the continuation of antimicrobial therapy.

A recent study showed that undertreatment is associated with an increased mortality rate.³⁶ In this study, all patients in the group administered with an inappropriate dose of antimicrobials were undertreated. Therefore, the use of an adequate dose of antimicrobials, according to the JRS guidelines, should be promoted. Further, it has been reported that prolonged administration of antimicrobials reduces the reinfection rate, whereas the risk of emergence of multidrug-resistant organisms increases.³⁷ In fact, all patients belonging to the group with a wrong dosing duration received it for more than 10 days, and the recurrence rate of aspiration pneumonia in this group was higher than the group with right dosing duration. However, it is unclear whether reinfection is caused by multidrug-resistant organisms.

This study had some limitations that should be considered. This was a single-center retrospective observational study, and the number of cases in the subgroup was limited. In addition,

judgments of appropriateness were investigated based on information obtained from medical records, and therefore, patients should be classified as inappropriate may in fact be classified as appropriate because of interpretation of data and evidences or lack of data, and vice versa.

CONCLUSIONS

This study shows that adherence to guidelines for antimicrobial therapy for patients with aspiration pneumonia in elderly nursing homes may contribute to improved clinical effectiveness. Further large-scale research should be conducted to clarify the appropriate use of antimicrobials.

ABBREVIATIONS

CAP, community-acquired pneumonia; q-SOFA, quick Sepsis Related Organ Failure Assessment; WBC, white blood cell; CRP, C-reactive protein; CTCAE, Common Terminology Criteria for Adverse Events; AST, aspartate transaminase; ALT, alanine transaminase; γ -GTP, γ -glutamyl transpeptidase; SCr, serum creatinine; eGFR, estimated glomerular filtration rate; NHCAP, nursing- and healthcare-associated pneumonia; HCAP, healthcare-associated pneumonia

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the ethics committee of Mie University Hospital (No. H2022-128).

AUTHORSHIP STATEMENT

All authors meet the ICMJE authorship criteria.

CONFLICTS OF INTEREST

None of the authors have financial or non-financial competing interests.

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Yuji Nakagawa: Conceptualization, Data curation, Formal Analysis, Methodology, Investigation, Writing – original draft; Hideo Kato: Validation, Writing – review & editing; Takuya Iwamoto: Writing – review & editing, , Project administration, Supervision.



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