Clinical effect of sulbactam/ampicillin on community-acquired pneumonia with positive *Streptococcus pneumoniae* urinary antigen test

Niro OKIMOTO, Koichi UCHIDA, Tadashi KATOH, Hisataka TANAKA
Toshikiyo HAYASHI, Takeyuki KURIHARA, Naoyuki MIYASHITA

Department of General Internal Medicine 1, Kawasaki Hospital, Kawasaki Medical School, 2-1-80, Nakasange, Kitaku, Okayama, 700-8505, Japan

ABSTRACT We investigated the efficacy of intravenous penicillin (sulbactam/ampicillin: SBT/ABPC) in adult patients with positive *Streptococcus pneumoniae* urinary antigen test requiring hospitalization. We administered 3g of SBT/ABPC intravenously in the morning and evening for 7-14 days to 32 adult community-acquired pneumonia patients with positive Binax NOW® *S. pneumoniae* urinary antigen. Clinical efficacy, bacteriological efficacy, and side effects of these patients were prospectively examined. We observed clinical efficacy in a total of 28 of 32 patients (87.5%); 24 of 26 moderate patients (92.3%), and four of six severe patients (66.7%). Side effects were drug eruption, increased GOT, increased AMY, and decreased WBC, observed in one patient each; however, all were mild. SBT/ABPC is extremely useful in patients with positive *S. pneumoniae* urinary antigen test requiring hospitalization

(Accepted on February 12, 2013)

Key words：***Stereptococcus pneumoniae* urinary antigen test, sulbactam/ampicillin**

INTRODUCTION

The JRS guidelines for the management of community-acquired pneumonia in adults recommend intravenous penicillin drip if *Streptococcus pneumoniae* urinary antigen test shows positive. Therefore, we examined the clinical efficacy of intravenous penicillin (sulbactam/ampicillin: SBT/ABPC) in patients with adult community-acquired pneumonia and positive *S. pneumoniae* urinary antigen test requiring hospitalization.

SUBJECTS AND METHODS

Subjects

Subjects were 32 patients with adult community-acquired pneumonia and positive *S. pneumoniae* urinary antigen test who underwent treatment at Kawasaki Hospital, Kawasaki Medical School from January 2009 through December 2011.

Methods

Adult community-acquired pneumonia patients with positive urinary antigen for *S.pneumoniae* (Binax NOW® *S. pneumoniae*) were administered

Corresponding author
Niro Okimoto
Department of General Internal Medicine 1, Kawasaki Hospital, Kawasaki Medical School, 2-1-80, Nakasange, Kitaku, Okayama, 700-8505, Japan
Phone : 81 86 225 2111
Fax : 81 86 224 6555
E-mail: n.okimoto@med.kawasaki-m.ac.jp

3g of SBT/ABPC intravenously in the morning and evening for 7-14 days. Then clinical efficacy, bacteriological efficacy, and side effects of these patients were prospectively examined. This study was approved by the clinical trial review committee of our institution.

RESULTS

Subjects (Table1)

Subjects were 20 males and 12 females aged 40 to 91 years (72.8 ± 15.5 years).

Severity by A-DROP system was moderate in 26 patients and severe in 6 patients.

Underlying disease (Table2)

COPD (chronic obstructive pulmonary disease) was observed in four subjects, bronchial asthma in three, bronchiectasis in three, cerebrovascular diseases in five, hypertension in five, diabetes mellitus in three, and hypothyroidism in one.

Clinical efficacy (Table3)

Clinical efficacy was observed in a total of 28 of 32 (87.5%) patients; 24 of 26 (92.3%) moderate patients, and in four of six (66.7%) severe patients. Efficacy was observed in three patients (PISP two, PRSP one) with penicillin-resistant *S. pneumoniae*. With regard to sensitivity of penicillin-G , MIC ≦2 μg , MIC =4 μg , and MIC ≧8 μg were judged as PSSP, PISP, and PRSP, respectively.

Bacteriological efficacy (Table 4)

PSSP 19 strains, PISP two strains, and PRSP one strain were isolated, and all were eradicated.

Side effects (Table 5)

Clinical adverse reaction was drug eruption in one patient (3.1%). Abnormal laboratory findings were increased GOT, increased AMY, and decreased WBC in one patient each; however, all were mild, and there were no patients whose treatment was discontinued, or who received treatment for adverse effects.

Table 1. Subjects

No. of patients	32 (M 20 : F 12)
AGE (years)	40-91 (72.8 ± 15.5)
Severity	
Moderate	26
Severe	6

Table 2. Underlying diseases

Respiratory diseases	10
Chronic obstructive pulmonary disease	4
Bronchial asthma	3
Bronchiectasis	3
Cerebrouasmlar diseases	5
Hypertension	5
Diabets mellitus	3
Hypothyroidism	1
None	8

Table 3. Clinical efficacy

Severity	Good	Poor	Efficacy rate (%)
Moderate: 26	24 (1)	2	92.3
Severe : 6	4 (2)	2	66.7
Total : 32	28	4	87.5

(1) PISP
(2) PRSP

Table 4. Bacteriological efficacy

	No. of strains	Eradicated	Eradication rate (%)
PSSP	19	19	
PISP	2	2	
PRSP	1	1	
Total	22	22	100%

Table 5. Side effects

Clinical adverse reaction	Drug eruption (1 / 32 = 3.1%)	1
Abnormal laboratory findings	GOT ↑	1
	Amy ↑	1
	WBC ↓	1
	(3 / 32 = 9.3%)	

DISCUSSION

S. pneumoniae is the most frequently observed microorganism in adult community-acquired pneumonia, accounting for 25-39% of patients with pneumonia requiring hospitalization. Pneumonia caused by *S. pneumoniae* is a potentially-severe pneumonia[1].

Gram staining and culture are useful in diagnosis. Recently, *S. pneumoniae* urinary antigen test has been widely used in the clinical setting for rapid diagnosis. The JRS guidelines for the management of community-acquired pneumonia in adults

recommend *S. pneumoniae* urinary antigen test to identify the causative organism. *S. pneumoniae* urinary antigen test (Binax NOW® *S. pneumoniae*) is the method to detect urinary capsule antigen for *S. pneumoniae* by immunochromatography. It has higher sensitivity than sputum or blood culture, with a sensitivity of 70-80% and a specificity of 80-90%[2-5]. The JRS guidelines also recommend intravenous penicillin for patients with positive *S. pneumoniae* urinary antigen test requiring hospitalization.

Therefore, we evaluated the efficacy of intravenous penicillin (sulbactam/ampicillin: SBT/ABPC) in patients with positive *S. pneumoniae* urinary antigen test requiring hospitalization. SBT/ABPC is ABPC compounded with a β-lactamase inhibitory agent that exhibits a strong antibacterial effect against *S. pneumoniae*.

Subjects were 26 moderate and 6 severe patients aged 40 to 91 years (72.8 ± 15.5years). Many patients had underlying respiratory diseases such as COPD, bronchial asthma, or bronchiectasis, suggesting that pneumonia caused by *S. pneumoniae* tends to occur in elderly individuals with chronic respiratory diseases.

Studies on the effect of SBT/ABPC on adult community-acquired pneumonia include an investigation by Williams *et al*.[6] reporting a higher efficacy than cefamandole in 36 of 37 (97%) patients, and an investigation by Seki *et al*.[7] reporting the same degree of efficacy as PIPC in 33 of 49 (67.3) patients. Studies on community-acquired pneumonia in the elderly include our report[8] of efficacy in 64 of 83 (77.1%) patients aged 75 years or greater, and an investigation by Yanagihara *et al*.[9] describing the same efficacy as IPM/CS in 32 of 35 (91.4%) patients aged 65 years or greater.

The present investigation of community-acquired pneumonia caused by *S. pneumoniae* alone revealed an excellent clinical effect with efficacy in 28 of 32 (87.5%) patients; 24 of 26 (92.3%) moderate patients, and four of six (66.7%) severe patients. Furthermore, in terms of bacteriology, all strains composed of PSSP (19 strains), PISP (two strains), and PRSP (one strain) were eradicatd.

Although the MIC of penicillin-G was as high as 4μ g[10] for PISP and PRSP, administration of 3 g of SBT/ABPC b. i. d. was efficacious for penicillin-resistant *S.pneumoniae*.

Side effects were drug eruption, increased GOT, increased AMY, and decreased WBC in one patient each; however, all were mild, showing high safety. The results of Metaanalysis[11] also showed high safety.

As shown above, intravenous penicillin (sulbactam/ampicillin: SBT/ABPC) for patients with positive *S. pneumoniae* urinary antigen test requiring hospitalization is extremely useful.

REFERENCES

1) The committee for JRS guideline in management of respiratory infections. The JRS Guidelines for the Management of Community-Acquired Pneumonia in adults. Tokyo, Kyorinsya. 2005, pp4-5.

2) Murdoch DR, Laing RT, Mills GD, Keralus NC, Town GJ, Mirrett S, Reller LB: Evaluation of rapid immunochromatographic test for detection of *Streptococcus pneumoniae* antigen in urine samples from adults with community-acquired pneumonia. J Clin Microbiol 39: 3495-3498, 2001

3) Smith MD, Derrington P, Evans R, Creek M, Morris R, Dance DA, Cartwright K: Rapid diagnosis of bacteremic Pneumococcal infections in adults by using the Binax NOW *Streptococcus pneumoniae* urinary antigen test: a prospective, controlled clinical evaluation. J Clin Microbiol 41: 2810-2813, 2003

4) Dominguez J, Gali N, Blanco S, Pedroso P, Prat C, Matas L, Ausina V: Detection of *Streptococcus pneumoniae* antigen by a rapid Immunochromatographic assay in urine samples. Chest 119: 243-249, 2001

5) Okimoto N, Hayashi T, Ishiga M, Nanba F, Kishimoto M, Yagi S, Kurihara T, Asaoka N, Tamada S: Positive duration of *Streptococcus pneumoniae* urinary antigen test. Medical Postgraduate 47: 294-296, 2009

6）Williams D, Perri M, Zervos MJ: Randomized comparative trial with ampicillin/sulbactam versus cefamandole in the therapy of community acquired pneumonia. Eur J Clin Microbiol Infect Dis 13: 293-298, 1994

7）Seki M, Higashiyama Y, Imamura Y, *et al*.: A clinical comparative study of piperacillin and sulbactam/ampicillin in patients with community-acquired bacterial pneumonia: Intern Med 48: 49-55, 2009

8）Okimoto N, Kurihara T, Honda N, Asaoka N, Fujita K, Ohba H, Nakamura J: Clinical effect of ampicillin with β-lactamase inhibitor(sulbactam/ampicillin) on community-acquired pneumonia in the elderly. J Infect Chemother 9: 183-186, 2003

9）Yanagihara K, Fukuda Y, Seki M, *et al*.: Clinical comparative study of sulbactam/ampicillin and imipenem/cilastatin in elderly patients with community-acquired pneumonia. Intern Med 45: 995-999, 2006

10）Niki Y, Hanaki H, Matsumoto T, *et al*.: Nationwide surveillance of bacterial respiratory pathogens conducted by the Japanese Society Of Chemotherapy in 2008: general view of the pathogens' antibacterial susceptibility. J Infect Chemother 17: 510-523, 2011

11）Zervos MJ, Skupien D, Dmuchowski CF: Metaanalysis of the efficacy and safety of ampicillin/sulbactam in the treatment of patients with bacterial infections of the lower respiratory tract. Infect Dis Clin Pract 6: 473-481, 1997