ORIGINAL CONTRIBUTION

Incidence of Methicillin-resistant Staphylococcus Aureus (MRSA) Isolation in a Geriatric Hospital: A Second Report on the Risk Factors for the Occurrence of MRSA Infection in the Elderly

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From April 1992 to March 1993, we examined the results of a bacterial culture from various clinical aspects in 83 elderly inpatients at a geriatric hospital. A case control study was carried out in order to evaluate the various factors which may influence the occurrence of methicillin-resistant Staphylococcus aureus (MRSA) infection. A univariate analysis revealed that a lower ADL score, a great number of antibiotics administration or the use of the third generation cephems increased the risk for MRSA infection. However, a multivariate analysis revealed that the risk for MRSA infection increased only among the patients who received the third generation cephems (OR: 2.80, 95% CI: 1.40-5.63). Therefore, in the elderly, the use of third generation cephems seems to pose a great risk factor for MRSA infection.

The level of total cholesterol, serum albumin or hemoglobin did not differ between the MRSA group and the non-MRSA group. However, among the patients who did not receive the third generation cephems, hypoalbuminemia was a risk for MRSA infection (OR: 2.06, 95% CI: 1.10-3.85). J Epidemiol, 1994; 4: 129-132.

MRSA, ADL, elderly, albumin, the third generation of cephems

The first strains of methicillin-resistant Staphylococcus aureus (MRSA) were reported in the United Kingdom in 1961, only two years after the introduction of methicillin1). Since then, similar strains have also been isolated in other parts of the world2,3) including Japan4). Since MRSA represents a high level of resistance for all antibiotics except for a few such as vancomycin and arbekacin5), the development of various MRSA strains has become a serious clinical problem as a causative pathogen of nosocomial infections. In particular, elderly patients have been reported to be one of the high risk groups for MRSA infection6). It is, therefore, an urgent problem to reduce the incidence of MRSA infection in geriatric hospitals.

Our previous study7) showed that inability to perform the activities of daily living (ADL) is one of the important risk factors for MRSA infection in the elderly. However, no analysis of the nutritional status, such as the presence of hypoalbuminemia, was provided in the previous paper. Furthermore, the previous study7) also raised the question as to whether the use of third generation cephems or the use of various antibiotics is a risk for MRSA infection. The purpose of the present study is to evaluate the effect of hypoalbuminemia, a low ADL score, the use of various antibiotics and the use of third generation cephems on the occurrence of MRSA infection.

SUBJECTS AND METHODS

In a geriatric hospital, which consisted of internal medicine ward and psychiatric ward for dementia, eighty-

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three elderly inpatients underwent a bacterial culture in the various clinical aspects from April 1992 to March 1993, whose materials included sputum, urine, stool, pus from a decubital ulcer and blood (Table 1).

In order to evaluate the various factors which may influence the occurrence of MRSA infection, a case control study was carried out. Some factors which may influence the occurrence of MRSA were investigated. The factors investigated were the number of antibiotics administered prior to the bacterial culture, the use of third generation cephameds, the age and sex of the patients, an evaluation of the activities of daily living (ADL) at the time of the bacterial culture and the nutritional state as expressed by the total cholesterol, serum albumin or hemoglobin. The number of antibiotics administered and the ADL score were determined in the same manners as that described in the previous study. Any antibiotics administered more than three days and within two weeks prior to the bacterial culture were counted as one antibiotic administered. When materials were examined for a bacterial culture more than two times, the number of antibiotics administered was the number of antibiotics prior to the first isolation of MRSA in MRSA positive patients while it was the maximum number of antibiotics administered in MRSA negative patients. The ADL score was calculated as the sum of the abilities to successfully perform ADL.

Those who could take meals by themselves received one point for meals, those who could walk by themselves got one point for movement and those who could urinate and have bowel movements by themselves were given one point for rest room function.

Table 1. Materials for bacterial cultures from inpatients.

| Group    | Sputum | Urine | Decubital ulcer | Others | Total |
|----------|--------|-------|-----------------|--------|-------|
| MRSA (+) | 21     | 4     | 4               | 0      | 29    |
| MRSA (−) | 23     | 27    | 0               | 4      | 54    |

The diagnosis of MRSA was made by Showa monodisc method. S. aureus, which showed resistance to both methicillin and ceftizixime, was diagnosed as MRSA. Serum albumin was measured by using autoanalyzer (Olympus, Tokyo) and hemoglobin was measured by the cyanmethemoglobin method.

A statistical analysis was performed using the Statistical Analysis System package (SAS Institute Inc.). Significance was determined by the Wilcoxon test and the chi-square test. A logistic regression analysis was used to control possible confounding factors of the serum albumin, ADL score, the number of antibiotics used prior to the bacterial culture and the use of third generation cephems on the occurrence of MRSA infection. The odds ratios (ORs) and their 95% confidence intervals (95% CIs) were then calculated for each factor on the basis of the logistic regression coefficient and its standard error.

RESULTS

Compared to the non-MRSA group, the ADL score was significantly lower in the MRSA group \( (p<0.05) \), the number of antibiotics used prior to the bacterial culture was significantly greater for the MRSA group \( (p<0.01) \) and third generation cephems were also used more commonly for the MRSA group \( (p<0.01) \) (Table 2). The level of total cholesterol, serum albumin or hemoglobin was found to be similar between the two groups.

After controlling for any confounding factors, the OR of patients who received third generation cephems was significantly higher than that of patients who did not \( (\text{OR: } 2.80, \text{ 95%CI: } 1.40-5.63) \) (Table 3).

Among the patients who received third generation cephems, none of patients with either a limited ADL, hypoalbuminemia or anemia demonstrated an increased risk for MRSA infection (Table 4). In contrast, among the patients who did not receive third generation cephems, those with hypoalbuminemia did show an increased risk of
MRSA infection (OR : 2.06, 95% CI : 1.10–3.85) (Table 5).

**DISCUSSION**

In the present study, the ADL score was lower in the MRSA group than in the non-MRSA group (p<0.05) (Table 2). Patients with a limited ADL may have a greater chance to receive an indwelling catheter. Since the use of an indwelling catheter is reported to be a risk for infection⁹, such patients are likely to receive a large amount of antibiotics. In addition, MRSA infection may occur more often in the patients with a limited ADL, who need frequent help in their daily lives and thus come in contact with numerous other people many times a day¹⁰. In the present study, the MRSA positive patients had a lower ADL score, and received a greater number of antibiotics prior to the bacterial culture than in the MRSA negative patients as reported previously⁷.

In Japan, the isolation of MRSA has dramatically increased since 1982 when third generation cephems were introduced⁴. Since most MRSA isolates are multiply resistant to various antibiotics⁴, the development of MRSA has become a serious clinical problem and is a causative pathogen of nosocomial infections. Methicillin resistance in staphylococci may be explained by the development of several alterations in the penicillin-binding proteins (PBP)s). The experimental study revealed that MRSA strains can grow in the presence of beta-lactam antibiotics because of the low affinities of the specific new PBP fraction (PBP2') for various beta-lactam antibiotics¹². Matsumoto¹³ described that the common use of third generation cephems, which have a weak antibacterial effect for Staphylococcus aureus, must have induced the rapid development of MRSA. In the present study, third generation cephems were used more commonly in the MRSA group than in the non-MRSA group as reported previously⁷. The result of our epidemiological study confirms that the use of third generation cephems is clearly

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**Table 3.** The odds ratio of the occurrence of MRSA infection among the inpatients in a geriatric hospital.
Cases: MRSA (+) n=29, Controls: MRSA (-) n=54

| Factors                          | OR     | 95% CI   |
|----------------------------------|--------|----------|
| Serum albumin                    | <3.5 g/dl vs 3.5 g/dl + | 1.53 | 0.88-2.66 |
| The ADL score at the time of the bacterial culture | 0 vs 1-3 | 1.17 | 0.65-2.09 |
| No. of antibiotics used prior to the bacterial culture | 3+ vs 0-2 | 1.14 | 0.46-2.81 |
| Use of 3rd generation cephems    | (+) vs (-) | 2.80** | 1.40-5.63 |

OR : odds ratio, 95% CI : 95% confidence interval, ** : p<0.01
ADL : activities of daily living

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**Table 4.** The odds ratio of the occurrence of MRSA infection among the patients who received generation cephems.
Cases: MRSA (+) n=25, Controls: MRSA (-) n=7

| Factors                          | OR     | 95% CI   |
|----------------------------------|--------|----------|
| Serum albumin                    | <3.5 g/dl vs 3.5 g/dl + | 0.48 | 0.14-1.69 |
| The ADL score at the time of the bacterial culture | 0 vs 1-3 | 0.94 | 0.22-4.10 |
| No. of antibiotics used prior to the bacterial culture | 3+ vs 0-2 | 1.06 | 0.24-4.60 |

OR : odds ratio, 95% CI : 95% confidence interval
ADL : activities of daily living

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**Table 5.** The odds ratio of the occurrence of MRSA infection among the patients who did not receive third generation cephems.
Cases: MRSA (+) n=2, Controls: MRSA (-) n=47

| Factors                          | OR     | 95% CI   |
|----------------------------------|--------|----------|
| Serum albumin                    | <3.5 g/dl vs 3.5 g/dl + | 2.06* | 1.10-3.85 |
| The ADL score at the time of the bacterial culture | 0 vs 1-3 | 1.05 | 0.55-2.02 |
| No. of antibiotics used prior to the bacterial culture | 3+ vs 0-2 | 1.47 | 0.45-4.77 |

OR : odds ratio, 95% CI : 95% confidence interval, * : p<0.05
ADL : activities of daily living
a risk factor for MRSA infection.

In the present study, MRSA positive patients received a greater number of antibiotics than negative patients. However, the multivariate analysis revealed that the use of third generation cephems was a risk factor for MRSA infection while the use of a large number of antibiotics was not. The result suggests that the use of the third generation of cephems rather than a great number of antibiotics may be an important risk factor for MRSA infection in the elderly.

Hypoalbuminemia has been suggested to be associated with limitations in ADL in the elderly population\(^{14,15}\). In the present study, however, the level of serum albumin was not different between patients with an ADL score 0 (n=40) and those with an ADL score ranging from 1-3 (n=43) (3.7±0.5 vs 3.8±0.4 g/dl, NS). This finding may be explained by the following possibilities. Firstly, the dehydration associated with fever may elevate the serum albumin level. Secondly, the patients who have good dining care may thus be in a good nutritional condition regardless of a limited ADL. Thirdly, the patients with liver cirrhosis, nephrotic syndrome or malignancy may have hypoalbuminemia regardless of their ADL abilities.

In the present study, the ADL score was significantly lower in the MRSA group than in the non-MRSA group while the serum albumin level was not. However, among the patients who did not receive third generation cephems, hypoalbuminemia was found to be an independent attributable risk for MRSA infection instead of a limited ADL. These results suggest that hypoalbuminemia may be a more important risk factor for MRSA infection than a limited ADL among those who do not receive third generation cephems.

In the present study, hypoalbuminemia increased the risk of MRSA infection among the patients who did not receive third generation cephems, while it did not increase the risk among those who receive third generation cephems. The result may suggest the following possibilities. Firstly, the use of the third generation of cephems may induce the development of MRSA, while hypoalbuminemia may be a risk for crossinfection of MRSA. Secondly, the greatly increased risk for MRSA infection after the administration of third generation cephems might therefore conceal the relationship between hypoalbuminemia and the occurrence of MRSA infection.

Inamatsu and Masuda described that most of MRSA infection in the elderly were mixed infection and MRSA caused infectious disease only 10-20% of them\(^{18}\). In the present study, among 29 patients with MRSA positive, 19 patients showed coinfection with other bacteria such as P. Aeruginosa. Among these 19 patients, it was unclear whether the isolation of MRSA was MRSA infection or MRSA colonization.

In summary, the use of a large number of antibiotics, a limited ADL and hypoalbuminemia may all be risk factors for MRSA infection among elderly patients. However, the administration of third generation cephems seems to be the most important risk factor for MRSA infection in elderly patients. Since MRSA represents a high level of resistance for almost all antibiotics except for a few, such as vancomycin and arbekacin\(^ {10}\), physicians should thus avoid any unnecessary administration of third generation cephems when treating the elderly patients.

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