Risk Factors for Methicillin-resistant Staphylococcus Aureus (MRSA) Urinary Tract Infection in a Geriatric Hospital: A Matched Case-control Study

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A matched case control study on MRSA urinary tract infection was carried out. The purpose of our study was to evaluate the effect of the use of antibiotics, the use of the third generation cephems, the hypoalbuminemia and the indwelling of catheter on the occurrence of MRSA urinary tract infection among the elderly. From April 1991 to March 1994, there were 8 inpatients who were suffered from MRSA urinary tract infection, which were used as cases. The twenty four age-and ADL-matched inpatients with non-MRSA urinary tract infection, three controls per case, were used as controls. Compared to the non-MRSA patients, the MRSA patients had a larger amount of antibiotics prior to the bacterial culture (1.3±0.9 vs 0.3±0.6, mean±SD, p<0.05). The third generation cephems were more commonly used in the MRSA patients than in the non-MRSA patients (50.0% vs 4.2%, p<0.05). The level of serum albumin was significantly lower in the MRSA patients than in the non-MRSA patients (3.4±0.6 vs 4.0±0.4 g/dl, p<0.05). Even after controlling confounding factor such as hypoalbuminemia, the use of the third generation cephems was a risk for MRSA urinary tract infection among the elderly (OR: 3.37, 95% CI: 1.11-10.28). In the elderly, use of the third generation cephems seems to be an important risk factor for MRSA urinary tract infection. J Epidemiol, 1995; 5: 95-98.

MRSA, urinary tract infection, elderly, albumin, the third generation 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 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 MRSA strains has become a serious clinical problems as a causative pathogen of nosocomial infections. The 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 the disability to perform the activities of daily living (ADL) is one of the important risk factors for MRSA infection in the elderly. However, the analysis by the nutritional status such as hypoalbuminemia was not presented in that paper. In addition, most of materials, from which MRSA was isolated, were sputums and pus from decubital ulcers. The purpose of this study is to evaluate the effect of the hypoalbuminemia, the use of antibiotics, the use of the third generation cephems and the indwelling of catheter on the occurrence of MRSA urinary tract infection in the elderly after controlling the influence of age and ADL.
SUBJECTS AND METHODS

In a geriatric hospital, which consisted of internal medicine ward and psychiatric ward for dementia, two hundred and eighty five elderly inpatients underwent a bacterial culture in the various clinical aspects from April 1991 to March 1993, whose materials included sputum, urine, stool, pus from decubital ulcer and blood. There were 8 inpatients who suffered from MRSA urinary tract infection, which were used as cases. In order to evaluate the various factors which may influence the occurrence of MRSA urinary tract infection, a matched case control study was carried out. Among the patients with the non-MRSA urinary tract infection, the 24 controls, three controls per case, were randomly selected, matching of age and ADL for each case. All controls were matched for age within ±4 years and ADL score within ±1, respectively. Among the 24 control patients, 19 patients (79%) were exactly matched for ADL. The patients, whose urine sample was negative for MRSA but any other material such as sputum, blood or pus from decubital ulcer, was positive for MRSA, were not used as controls.

Several factors which may influence the occurrence of MRSA urinary tract infection were investigated. The factors investigated were the number of antibiotics administered prior to bacterial culture, use of the third generation cephems, the age and sex of the patients, the ADL score and the nutritional state expressed by serum albumin at the time of the bacterial culture, and the indwelling of catheter. The number of antibiotics administrated and the ADL score were determined after the manner of our previous study. Antibiotics administrated more than three days and within two weeks prior to the bacterial culture were counted as one. When materials were examined for a bacterial culture more than twice, the number of antibiotics represents the number of antibiotics prior to the first isolation of MRSA in MRSA positive patients and the maximum number of antibiotics administered in MRSA negative patients. The ADL score was the sum of the abilities to perform ADL, ranging from 0 to 3. The patients got one point for each ability to perform ADL, which was the ability to take meals, to walk or to urinate and have bowel movements.

The diagnosis of MRSA was made by Showa monodisc®. S. aureus, which showed resistance to both methicillin and cefotizoxime, was diagnosed as MRSA. Serum albumin was measured by autoanalyzer (Olympus, Tokyo).

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 for the possible confounding effects of serum albumin and the use of antibiotics or the use of the 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

Gender, age and ADL score did not differ between MRSA group and non-MRSA group. Compared to the non-MRSA group, the number of antibiotics used prior to the bacterial culture was significantly greater for the MRSA group (p<0.05) and the third generation cephems were used more commonly for the MRSA group (p<0.05) (Table 1). In contrast, serum albumin level was significantly lower in the MRSA group than in the non-MRSA group (p<0.05). The indwelling of catheter was more common in the MRSA group than in the non-MRSA group (25.0% vs 8.3%), but failed to show significant difference.

As shown in Tables 2, 3, the patients with hypoalbuminemia had an increased risk for MRSA infection after

| Table 1. Factors related to the occurrence of MRSA infection among the inpatients in the geriatric hospital. |
|-----------------------------------------------|-----------------------------------------------|-----------------|
| Male/Female                                   | MRSA (+) n=8 | MRSA (-) n=24 | p-value |
| Male/Female                                   | 3/5          | 6/18           | NS     |
| Age (years old)                               | 78.3 ± 7.8   | 79.3 ± 8.3     | NS     |
| ADL score at the time of the bacterial culture | 0.8 ± 1.2    | 0.8 ± 1.1      | NS     |
| No. of antibiotics used prior to the bacterial culture | 1.3 ± 0.9 | 0.3 ± 0.6 | <0.05 |
| Use of the 3rd generation of cephems           | 50.0%        | 4.2%           | <0.05 |
| Serum albumin (g/dl)                          | 3.4 ± 0.6    | 4.0 ± 0.4      | <0.05 |
| Catheter                                    | 25.0%        | 8.3%           | NS     |

Values are means ± SD. Catheter $: indwelling of catheter in the urinary tract.
Table 2. Odds ratio of the isolation of MRSA among the patients with urinary tract infection in the geriatric hospital (i).
Case: MRSA (+), n=8, Control: MRSA (-), n=24.

| Factors                | OR   | 95% CI       |
|------------------------|------|--------------|
| Serum albumin          | <3.5 g/dl vs 3.5 g/dl+ | 2.72# | 0.90-8.16    |
| Use of antibiotics     | (+) vs (-) | 2.03 | 0.77-5.34    |

OR: odds ratio, 95% CI: 95% confidence interval.
# : p<0.1

Table 3. Odds ratio of the isolation of MRSA among the patients with urinary tract infection in the geriatric hospital (ii).
Case: MRSA (+), n=8, Control: MRSA (-), n=24.

| Factors                | OR   | 95% CI       |
|------------------------|------|--------------|
| Serum albumin          | <3.5 g/dl vs 3.5 g/dl+ | 2.57# | 0.91-7.24    |
| Use of 3rd generation of cephems | (+) vs (-) | 3.37* | 1.11-10.28   |

OR: odds ratio, 95% CI: 95% confidence interval.
# : p<0.1, * : p<0.05

controlling the effect of the administration of antibiotics (OR : 2.72, 95% CI : 0.90-8.16) as well as the administration of the third generation cephems (OR : 2.57, 95% CI : 0.91-7.24). On the other hand, after controlling the effect of hypoalbuminemia, the OR of patients who had received the third generation cephems was significantly higher than that of patients who had not (OR : 3.37, 95% CI : 1.11-10.28) (Table 3).

**DISCUSSION**

MRSA infection may occur more often in the patients with a limited ADL, who need frequent help in their daily lives and come in contact with others many times a day. In the present study, MRSA positive patients received more kinds of antibiotics than negative patients. The result indicates that the use of many kinds of antibiotics is a risk factor for MRSA urinary tract infection without the influence of ADL.

In Japan, the frequency of the MRSA isolation has dramatically increased since 1982 when the third generation cephems were introduced. Since most of MRSA isolates represent a high level of resistance for all antibiotics except for a few such as vancomycin and arbekacin, the development of MRSA has become a serious clinical problem as a causative pathogen of nosocomial infections. Methicillin resistance in staphylococci may be explained by the several alterations of penicillin-binding proteins (PBPs). Utsui and Yokota suggested 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 antibiotics.

Matsumoto described that the common use of the third generation of cephems, which have a weak antibacterial effect for Staphylococcus aureus, must have induced the development of MRSA. In the present study, the third generation cephems were twelve times more commonly used in the MRSA group than in the non-MRSA group (50.0% vs 4.2%, p<0.05). The result confirms that the administration of the third generation cephems is an important risk factor for MRSA infection.

Hypoalbuminemia is suggested to associate with limitations in ADL in the elderly population. In the present study, however, the level of serum albumin was significantly lower in the MRSA group than in the non-MRSA group without the influence of ADL (Table 1). In addition, the average of serum albumin level in the MRSA group was lower compared to the reference range of serum albumin level (3.5-5.0 g/dl).

Either antibiotics induced liver damages or long lasting infections may cause hypoalbuminemia in the MRSA group patients, who had been suffered from long lasting infections in spite of antibiotics administration and received a great number of antibiotics before the isolation of MRSA.

In the present study, hypoalbuminemia increased the risk of MRSA infection after the controlling the effect of use of antibiotics or the administration of the third generation cephems which were used only in the cases whose bacterial infections were resistant to other kinds of antibiotics (Table 2). These results suggest that hypoalbuminemia is an independent risk factor for MRSA urinary tract infection.

Konn described that the indwelling of catheter is a risk factor for MRSA infection. In the present study, the rate of patients with the indwelling of catheter in the MRSA group was three times as great as the non-MRSA group (25.0% vs 8.3%), but failed to show the significant difference. A small number of MRSA positive cases in the present study may explain this result.

In summary, hypoalbuminemia, the use of many kinds of antibiotics and the use of the third generation cephems may be risk factors for MRSA urinary tract infection among the elderly patients. Physicians should avoid any unnecessary administration of antibiotics in treating the elderly patients. Furthermore, physicians should avoid the third generation cephems when they can use antibiotics other than the third generation cephems.

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