# Outcome comparison of ampicillin/sulbactam or amoxicillin/clavulanate vs. 3rd generation cephalosporin against community-acquired pneumonia

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## Background

Use of penicillin class (such as ampicillin/sulbactam or amoxicillin /clavulanate) is included in a treatment guideline of community-acquired pneumonia (CAP). However, the use of the wide spectrum antibiotics such as 3rd generation cephalosporin is common in the clinical practice. This practice can enhance the problems of antimicrobial resistance and high medical expenses.

## Method

The case-control study was performed. We did random matching at a ratio of 1:2 (age; ±5 years, sex; same) for ampicillin/sulbactam or amoxicillin/clavulanate: 3rd generation cephalosporin as empiric antibiotics for patients with CAP. The patients enrolled in this study were between Jan. 2010 and Jun. 2012. The hospitals participated in this study were 4 academic hospitals in Korea.

## Results

We enrolled 225 patients (ampicillin/sulbactam: 72, amoxicillin/ clavulanate: 3, 3rd generation cephalosporin: 150). The average age was 60.4 (minimum 19, maximum 90). We compared the selection bias of choice of empiric antibiotics (penicillin group vs. 3rd generation cephalosporin) that might related with severity of CAP (Table 1)

Table 1. Hospitals and patients investigated (matching 1:2)

| Hospital | Penicillins | 3rd Generation Cephalosporins | Total |
|---|---|---|---|
| KNUH CAP Cohort | 42 | 84 | 126 |
| Kyemyung University Hospital | 10 | 20 | 30 |
| Korea University Hospital, Anam | 20 | 40 | 60 |
| Youngnam University Hospital | 3 | 6 | 9 |
| Total | 75 | 150 | 225 |

CURB-65 of penicillin group vs. 3rd generation cephalosporin were 1.17±1.05, 1.07±0.95 (p=0.487), respectively, and Pneumonia Severity Index (PSI) were 77.5±28.2, 74.7±29.3 (p=0.50), respectively. This means the differences in the selection of penicillin group or 3rd generation as empiric therapy for CAP in this study.

Table 2. Macrolide or fluoroquinolone combination in the CAP patients treated with penicillins vs. 3rd generation cephalosporins (Chi-square test, p=0.009)

| | | Penicillins | 3rd Generation Cephalosporins | Total |
|---|---|---|---|---|
| Combination vs. monotherapy | Combination therapy | 51 | 126 | 177 |
| | | 68.0% | 84.0% | 78.7% |
| | Monotherapy | 24 | 24 | 48 |
| | | 32.0% | 16.0% | 21.3% |
| Total | | 75 | 150 | 225 |

However, there was statistically significant difference between both groups in the combination of macrolide or quinolone; penicillin group 68.0% (51/75) vs. 3rd generation cephalosporin 84% (126/150)(p=0.009) (Table 2).

The 'early failure' judged at 72 hours after treatment in penicillin group vs. 3rd generation cephalosporin was 13.3% (20/150) vs. 21.38% (16/75)(p=0.128), respectively. Overall outcome as treatment failure judged at 30 days in penicillin group vs. 3rd generation cephalosporin was 2.7% (2/75), 1.3% (2/150) and was not statistically significant (Table 3)

Table 3. Comparison of rate of early failure in the CAP patients treated with penicillins vs. 3rd generation cephalosporins (Chi-square test, p=0.128)

| | Clinical and radiological improvement without modification of initial antibiotics | Early failure | Total |
|---|---|---|---|
| Penicillins | 59 | 16 | 75 |
| | 78.7% | 21.3% | 100.0% |
| 3rd Generation Cephalosporins | 130 | 20 | 150 |
| | 86.7% | 13.3% | 100.0% |
| Total | 189 | 36 | 225 |

Additionally we conducted multivariate logistic regression analysis with variables (empiric antibiotics, age, Charlson comorbidity score, presence of combination treatment, PSI score, etc.). In this analysis, PSI was significant (p=0.022), and use of ampicillin/sulbactam or amoxicillin/clavulanate did not show significance of early failure (OR 1.68, 95% CI: 0.79-3.57, p=0.181)(Table 4)

Table 4. Multivariate logistic regression analysis for risk factors of early failure

| | OR | 95% CI | | p-value |
|---|---|---|---|---|
| Penicillins/3rd Generation Cephalosporins | 1.676 | 0.787 | 3.569 | 0.181 |
| PSI score | 1.024 | 1.003 | 1.044 | 0.022 |
| Charlson comorbidity score | 0.860 | 0.708 | 1.045 | 0.129 |
| Age | 0.985 | 0.952 | 1.019 | 0.387 |
| Combination therapy | 0.688 | 0.297 | 1.595 | 0.383 |

## Discussion and conclusion

This study had a limitation of a relatively small number of patients. In the view of antibiotic stewardship, we are in need of reducing the use of wide-spectrum antibiotics. Low mortality rate of CAP (penicillin group vs. 3rd generation cephalosporin group in 30-day mortality of 2.7% and 1.3%, respectively) in this study supports that use of relatively narrow spectrum antibiotics for the empiric antibiotic use against CAP.

This case-control study showed that ampicillin/sulbactam or amoxicillin/clavulanate might be not inferior to 3rd generation cephalosporin for the treatment of CAP and could be used with low risk of treatment failure.