ABSTRACT

Background: Siriraj Hospital has implemented post-authorization of target antibiotics (piperacillin/tazobactam, meropenem, imipenem/cilastatin and doripenem) for nearly 10 years. Currently, antibiotic approval is implemented by ID clinical fellows.

Methods: During Feb – Sep 2013, we conducted a cluster randomized controlled trial in 6 general medical wards at Siriraj hospital to compare antibiotic approval by ID clinical fellows vs. trained general pharmacists in terms of clinical outcomes, microbiological outcomes and antibiotic consumption and expenditure. Three wards were assigned to the intervention group (the pharmacist group) while the other three wards were assigned to the control group (the fellow group). The target antibiotics can be prescribed by the responsible physicians during the first 72 hrs, after that an approval from the fellows or the pharmacists is required.

Results: There were 806 enrolled patients. The preliminary analysis included 178 patients in the pharmacist group and 168 patients with 181 prescriptions in the fellow group. Baseline characteristics of both groups were comparable.

Conclusion: Although the patients who received antibiotic approval by the pharmacists had significantly higher consumption of target antibiotics, there was no significant difference in antibiotic treatment outcomes. Therefore, the trained pharmacists could be an alternative to ID specialists for antibiotic approval in the limited setting. (ClinTrials.gov number, NCT 01797133)

BACKGROUND:

Siriraj Hospital has implemented post-authorization of target antibiotics (piperacillin/tazobactam, meropenem, imipenem/cilastatin and doripenem) for nearly 10 years. Currently, antibiotic approval is implemented by ID clinical fellows. Thailand has no official training for ID clinical pharmacist; therefore the number of ID clinical pharmacist is very limited. Majority of the ID clinical fellows are recruited after formal ID training. Given these considerations, we conducted a cluster randomized controlled trial to compare antibiotic approval by ID clinical fellows compared with trained general pharmacists in terms of clinical outcomes, microbiological outcomes, antibiotic consumption and expenditure.

METHODS:

Setting:

During Feb-1 Sep 2013, we conducted a cluster randomized controlled trial in 6 general medical wards at Siriraj hospital, Bangkok, Thailand. Siriraj hospital is a 2200-bed university hospitals and a largest referral center in Thailand. The study was approved by the Siriraj Institutional Review Board with waiver of informed consent.

Participants:

In total, 168 patients who received at least 1 dose of target antibiotic. A patient could be recruited into the study more than once if he/she received the target antibiotic to treat new episode of infection and the previous dose of the antibiotic was not given within 24 hours.

Randomization and Study Intervention:

Three wards were randomly assigned to the intervention group while the other three wards were assigned to the control group.

RESULTS:

Data collection on antibiotic consumption was directly retrieved from the pharmacy database while all other data was retrieved by chart review.

A. Antibiotic approval by ID clinical fellows (Standard of care; the control group):

Antibiotic approval was performed by the responsible physicians; it was not reviewed by the ID clinical fellows. The antibiotic approval process took 67.70 ± 22.09 hours. After that, the prescription requires approval. Antibiotic approval is signed by the ID clinical fellow, the ID chief fellow and the ID faculty supervision. The assessment can be divided into three categories.

1. Approved: If the target antibiotic was appropriately prescribed, it can be prescribed without further evaluation. After that, the responsible physician needs to apply for approval again.

2. Terminated approved for 3 days while waiting for additional information.

3. Not approved: If the target antibiotic was inappropriate prescribed, it must be reviewed. Furthermore, the responsible physician may be suggested to discuss the antibiotic prescription with the ID chief fellow. The ID clinical fellow can independently review the prescriptions. All of the doctor's and ID fellows' prescriptions need to be confirmed by the ID faculty.

B. Antibiotic approval by trained general pharmacists (the intervention group):

All processes were exactly the same as the control group except it was implemented by the ward pharmacists, under the ID faculty supervision.

STATISTICAL ANALYSIS:

Descriptive analysis and frequency tables were performed. Mean and standard deviation were used to describe continuous variables. Chi-square test was used to analyze categorical variables. In the analysis of the continuous outcome variables, the level of significance was 0.05. All statistical analyses were performed using the STATISTICA version 12.0 (StatSoft, Corp, College Station TX).

RESULTS:

Based on data from the pharmacy database, there were 420 prescriptions in the pharmacist group vs. 455 prescriptions the fellow group. Due to the technical failure, 171 patients (37%) of total patients were recruited in the pharmacist group (178 prescriptions) and 40% of patients in the fellow group (181 prescriptions).

Clinical characteristics were comparable between two groups. However, patients in the pharmacist group were more likely to be neutropenic (8.07% vs. 2.98%, P = 0.04), had previous use of urinary catheter (27.95% vs. 14.29%, P = 0.002), previous exposure to antimicrobial agent (56.52% vs. 45.24%, P = 0.04). In contrast, a significantly lower proportion of patients in the pharmacist group was diagnosed with autoimmune diseases during hospitalization (7.49% vs. 67.1%, P = 0.01).

More than 90% of patients in both groups had clinically-confirmed infection, and major drug-related adverse effects (69.29% vs. 57.46%, P = 0.55). The three leading sites of infection of both groups were lower respiratory tract infections (34.27% vs. 23.93%, P = 0.33), followed by urinary tract infections (23.03% vs. 20.44%, P = 0.55). Similarly in both groups, the most frequently-prescribed target antibiotics were meropenem (56.85% vs. 52.53%, P = 0.26) and doripenem (28.75% vs. 30.42%, P = 0.67). imipenem/cilastatin (0.08% vs. 6.63%, P = 0.51) and doripenem (0.43% vs. 0.99%, P = 0.31). None of these characteristics was statistically different.

Table 1. Antibiotic consumption and antibiotic expenditure (data from the Pharmacy database)

<table>
<thead>
<tr>
<th>Outcomes (per prescription)</th>
<th>Pharmacist (N = 420)</th>
<th>Fellow (N = 455)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDD of target antibiotics</td>
<td>11.76 ± 11.96</td>
<td>10.16 ± 9.50</td>
<td>0.02</td>
</tr>
<tr>
<td>Cost of target antibiotics, baht</td>
<td>8.99 ± 6.77</td>
<td>7.86 ± 5.72</td>
<td>0.04</td>
</tr>
<tr>
<td>Cost of antibiotic treatment, baht</td>
<td>11.86 ± 4.51</td>
<td>10.96 ± 6.97</td>
<td>0.035</td>
</tr>
</tbody>
</table>

CONCLUSION:

It has been demonstrated that the general pharmacists who have received the ID short course training could effectively implement the ASP using pre-authorization strategy, without compromising the patients' clinical outcomes. Although there was no significant difference in antibiotic treatment outcomes, the pharmacist group spent longer duration of antibiotic treatment. Given these findings, this strategy appears to be safe but may not be as efficient as the pre-authorization program implemented by the ID department. Therefore, the pharmacist-based pre-authorization may be considered as an acceptable alternative in the resource limited setting.

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