J Infect Chemother 22 (2016) 532–535

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Original article

# Impact of computerized pre-authorization of broad spectrum antibiotics in *Pseudomonas aeruginosa* at a children's hospital in Japan

Yuho Horikoshi [a, *], Hiroshi Higuchi [b], Junichi Suwa [c], Mihoko Isogai [a], Takayo Shoji [d], Kenta Ito [a]

[a] Division of Infectious Diseases, Department of Pediatrics, Tokyo Metropolitan Children's Medical Center, Japan
[b] Division of Microbiology, Department of Clinical Laboratory, Tokyo Metropolitan Children's Medical Center, Japan
[c] Department of Pharmacy, Tokyo Metropolitan Children's Medical Center, Japan
[d] Division of Pediatric Infectious Diseases, Shizuoka Children's Hospital, Japan

ARTICLE INFO

*Article history:*
Received 6 April 2016
Received in revised form
2 May 2016
Accepted 2 May 2016
Available online 2 June 2016

*Keywords:*
Antimicrobial stewardship program
Resistant organism
Pre-authorization
*Pseudomonas aeruginosa*
Carbapenems
Children's hospital

ABSTRACT

*Background:* The spread of antimicrobial-resistant organisms is a global concern. To stem this tide, an antimicrobial stewardship program at hospitals is essential to optimize the prescription of broad spectrum antibiotics. In this study we examined the impact of computerized pre-authorization for broad spectrum antibiotics for *Pseudomonas aeruginosa* at a children's hospital.

*Methods:* An antimicrobial stewardship program at Tokyo Metropolitan Children's Medical Center was assessed between March 2010 and March 2015. A paper-based post-prescription audit was switched to computerized pre-authorization for broad antipseudomonal agents in October 2011. The prescriber was required to obtain approval from physicians in the pediatric infectious diseases division before prescribing restricted antimicrobial agents. Approved prescriptions were processed and logged electronically. We evaluated days of therapy per 1000 patient-days, the cost of antibiotics, and the susceptibility of *P. aeruginosa* to piperacillin, ceftazidime, cefepime, piperacillin/tazobactam, carbapenems, and ciprofloxacin. Also, the average length of admission and infection-related mortality at 30 days were compared pre- and post-intervention.

*Results:* Administration of carbapenems, piperacillin/tazobactam, and ceftazidime decreased significantly after the introduction of computerized pre-authorization. Antibiotic costs were reduced by JPY2.86 million (USD 26,000) annually. None of the antipseudomonal agents showed decreased sensitivity. The average length of admission was shorter in post-intervention. Infection-related mortality at 30 days showed no difference between the pre- and post-intervention periods.

*Conclusion:* An antimicrobial stewardship program using computerized pre-authorization decreased the use and cost of broad spectrum antibiotics without significant difference in infection-related mortality at 30 days, although our study did not improve susceptibilities of *P. aeruginosa*.

© 2016 Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

## 1. Background

The spread of antimicrobial resistant organisms (AROs) is a serious threat to health requiring global attentions and interventions [1]. Infections by AROs result in worse clinical outcomes compared to infections by non-AROs, entail higher economic costs, and require more health care resources [2–5]. In particular, the spread of gram negative multi-drug resistant bacillus strains threatens a crisis of global proportions as the number of effective antimicrobial agents diminishes.

The carbapenem antimicrobials, now on the market for nearly three decades, are the last of the beta-lactam antibiotics with the broadest spectrum of activity against gram negative bacteria. Carbapenem use, however, has been associated with the emergence of multi-drug resistant organisms [6,7]. The resistance rate of *Pseudomonas aeruginosa* to meropenem reached 17.8% according to a national surveillance conducted in 2012 in Japan [8]. Currently,

* Corresponding author. 2-8-29 Musashidai Fuchu, Tokyo 183-8561, Japan. Tel.: +81 42 300 5111; fax: +81 42 312 8162.
*E-mail address:* yuho_horikoshi@tmhp.jp (Y. Horikoshi).

http://dx.doi.org/10.1016/j.jiac.2016.05.001
1341-321X/© 2016 Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

single therapy with carbapenem class antimicrobials is no longer considered to provide complete coverage against AROs.

The diminishing efficacy of antimicrobial drugs makes the establishment of an effective infection control team (ICT) and antimicrobial stewardship program (ASP) essential for controlling AROs in hospital settings. In Japan, hospitals were reimbursed by national health insurance for each admission since 2010, if hospitals were able to verify that appropriate ICT and ASP were being implemented at the time. The required ASP consisted of either pre-authorization for prescriptions or the auditing of broad spectrum antibiotics after prescription. Pre-authorization for prescriptions was clearly favored for enabling the immediate and direct influence of the targeted drugs. Delory et al. reported that pre-authorization in French hospitals significantly reduced the prescription of carbapenems compared to a post-prescription audit [9]. In Japan, 89% of children's hospitals implemented ASP in 2013, but only a quarter of those enforced pre-authorization of prescriptions [10]. The aim of our study is to evaluate the impact of the pre-authorization of broad spectrum antibiotics in a children's hospital.

## 2. Methods

The study was conducted at Tokyo Metropolitan Children's Medical Center in Japan, a tertiary children's hospital with 561 pediatric beds. The division of pediatric psychiatry (200 beds) was excluded from analysis, as they seldom prescribe antibiotic agents. The hospital opened in March 2010 with an ASP consisting of only a post-prescription audit for carbapenems. Physicians were required to submit a document reporting their prescription to ASP. The ASP team then reviewed the antibiotic treatment and de-escalation or discontinuation was proposed when appropriate. The ASP team consisted of specialists in pediatric infectious diseases, a pharmacist, and a microbiologist. Only the number of physicians increased during the study period from one in 2010, to three in 2011, five in 2012 and 2013, seven in 2014 and nine in 2015. In October, 2011, the ASP switched to requiring computerized pre-authorization for prescriptions of broad spectrum antibiotics. Medications were ordered via an electronic form, which automatically blocked any orders of restricted antimicrobial agents. The prescriber was then required to call a physician in the pediatric infectious diseases division to obtain approval for the prescription. If approval was granted, the block was lifted. Restricted antipseudomonal agents were designated by each division. Antipseudomonal agents used in our study were piperacillin, ceftazidime, cefepime, piperacillin/tazobactam, meropenem, imipenem/cilastatin, panipenem/betamipron, and ciprofloxacin. Imipenem/cilastatin and panipenem/betamipron were removed from the formulary during study period due to infrequent use. All divisions except hemato-oncology were barred from ordering cefepime, piperacillin/tazobactam, carbapenems, and ciprofloxacin. The division of hemato-oncology was restricted to ordering carbapenems and quinolones only for their immunocompromised patients. The pediatric intensive care unit (PICU) and neonatal intensive care unit (NICU) had no blocking system in their electronic forms for antibiotic orders, as their patients were often critically ill. Nonetheless pre-authorization was required. The paper-based post-prescription review period between March 2010 and September 2011 (phase 1) and the computerized pre-authorization period for prescriptions between October 2011 and March 2015 (phase 2) were then compared retrospectively. Antibiotic use density (AUD) was calculated by days of therapy (DOT) per 1000 patient-days. The DOTs of meropenem, imipenem/cilastatin, and panipenem/betamipron were combined as DOT for carbapenems. DOTs for antipseudomonal agents were compared between phase 1 and 2. The cost of antibiotic was calculated in terms of the number of ampules dispensed multiplied by the government-approved price of 2010. Japanese yen was converted to 1 United States dollar (USD) at rate of 110 yen. Susceptibility of *P aeruginosa* was interpreted using clinical laboratory standards institute M100-S25. The minimum inhibitory concentration was determined by MicroScan®WalkAway®-96plus system (Siemens, Germany). If *P aeruginosa* was isolated from multiple samples from same patient within 4 weeks, only the first isolate was analyzed to exclude the influence of frequent sampling. All-cause mortality cases during the study period were reviewed for infection-related mortality at 30 days. Infection-related mortality was defined as either microbiologically confirmed infections or clinical infections determined by staff pediatric infectious diseases' physician, which primarily resulted in death of patients due to dysfunction of vital organs. Patients in palliative care due to a primary disease were excluded from mortality analysis. Mann–Whitney U test was used for statistical analysis. SPSS statistics 22 (IBM, the USA) was used, and a P value of less than 0.05 was defined as significant. The institutional review board at Tokyo Metropolitan Children's Medical Center approved the study (H27b-57).

## 3. Results

The AUDs of carbapenems and piperacillin/tazobactam decreased significantly in phase 2. The AUDs of the other restricted antibiotics, cefepime and ciprofloxacin, did not show a significant decrease, although cefepime showed a tendency to a decline in use in phase 2 ($p = 0.096$). The AUD of the non-restricted antibiotic, ceftazidime, also decreased significantly, although this was not the case with piperacillin (Table 1).

The cost of antibiotics per 1000 patient-days for carbapenems and piperacillin/tazobactam was significantly lower in phase 2 (Table 2). The other antibiotics showed no difference.

None of the antibiotic susceptibility rates for *P aeruginosa* changed during the study periods although piperacillin tended to produce more resistant strains in phase 2. ($p = 0.066$) (Table 3).

The average length of hospitalization was shorter in phase 2. All-cause mortality and infection-related mortality at 30 days did not increase during the study periods (Table 4).

## 4. Discussions

The ASP based on pre-authorization significantly reduced the use of carbapenems and piperacillin/tazobactam by 47% and 57%, respectively. Restrictions on some antibiotics are known to cause increased use of others [11]. In our study, use of other antipseudomonal antibiotics did not increase in relation to either the restriction or non-restriction of the target antibiotics. Interestingly, unrestricted agent of ceftazidime decreased significantly ($p = 0.008$) and even piperacillin showed a tendency towards decreased use ($p = 0.068$). Ciprofloxacin was the only drug whose use did not decrease in phase 2. The use of ciprofloxacin was contraindicated in children in Japan during the study period and was

**Table 1**
DOTs per 1000 patient-days of antibiotics.

| | Phase 1 Average (SD) | Phase 2 Average (SD) | p value |
|---|---|---|---|
| Carbapenems | 7.38 (0.98) | 3.48 (0.40) | <0.001[a] |
| Piperacillin/Tazobactam | 6.27 (0.67) | 3.61 (0.32) | 0.001[a] |
| Cefepime | 19.6 (1.11) | 17.7 (0.94) | 0.096 |
| Ciprofloxacin | 1.30 (0.46) | 1.60 (0.27) | 0.317 |
| Ceftazidime | 5.51 (0.49) | 3.90 (0.28) | 0.008[a] |
| Piperacillin | 9.75 (0.83) | 8.15 (0.43) | 0.068 |

[a] Statistically significant.

Download English Version:

https://daneshyari.com/en/article/3376669

Download Persian Version:

https://daneshyari.com/article/3376669

Daneshyari.com