ICAP Journal Club

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Article

Dawaiwala I, Raut S, Fuse M, et al. Antimicrobial stewardship and clinical pharmacist interventions in an Indian tertiary care hospital. *Journal of the American College of Clinical Pharmacy* 2024;7:46-54.
https://accpjournals.onlinelibrary.wiley.com/doi/pdfdirect/10.1002/jac5.1885

Study Summary

This quasi-experimental study evaluated the type and acceptance rates of clinical pharmacist interventions, in the implementation of an antimicrobial stewardship program, and assessed its impact on antimicrobial utilization.

Study Setting

- An academic tertiary care hospital located in Pune, Maharashtra, India.
- The hospital had a 350-bed capacity including 60 intensive care unit (ICU) beds.

Methods

- The study included adult patients aged ≥18 years who were admitted to inpatient services. Patients who had been admitted to one of three ICUs dedicated to patients with COVID-19 and one ward dedicated to patients with COVID-19 were all excluded.
- The study had two distinct phases: pre-intervention and intervention.
- During the pre-intervention phase (April 2021-March 2022), clinical pharmacists were primarily engaged in monitoring antimicrobial consumption and collecting pertinent patient data without deploying any intervention.
- During the intervention phase (April 2022-March 2023), five antimicrobial stewardship measures were implemented:

    1. *Justification form:* Within 24 hours of initiating treatment with restricted antimicrobials, prescribing doctors were required to complete this form, providing a valid rationale for its use. The form included a QR code that provided access to the hospital's antibiogram data, antibiotic and surgical prophylaxis policy, and the World Health Organization (WHO) AWaRe antibiotic book.

2. *Prospective audit:* A clinical pharmacist audited the prescribed antimicrobials within 24 hours of their being issued, reviewing for guidelines concordance, therapeutic duplication, appropriateness as per pharmacokinetic parameters, and history of allergies. Prior to the review, the patient received initial doses of antimicrobials.
3. *Clinical pharmacist interventions:* Clinical pharmacists provided verbal feedback to the treating consultants, including proposing de-escalation of the antimicrobial to a narrow spectrum agent, switching to an unrestricted agent based on culture results after discussion with an infectious diseases physician, or discontinuing the antimicrobial if indicated.
4. *Training:* Three two-hour training sessions for clinicians and infection control nurses were conducted by an infectious disease physician, a clinical microbiologist, and a clinical pharmacist on: 1) the mechanism of action and spectrum of antimicrobial agents; 2) rationale for their use; and 3) mechanisms of resistance and indications of antimicrobial agents. Policy updates were disseminated via a WhatsApp group.
5. *Antimicrobial consumption data:* Antimicrobial consumption data were presented during monthly meetings of the infection control committee.

- The clinical pharmacist team consisted of five members, led by a clinical pharmacist with one year of specialized training in infectious disease clinical pharmacy and antimicrobial stewardship, under the guidance of an infectious disease physician. The remaining team members received three months of training in the same area.
    - Three clinical pharmacists allocated 50% (approximately 4 hours) of their time to the infectious disease clinical pharmacy.
    - Two clinical pharmacists dedicated 25% (approximately 2 hours) of their time to antimicrobial stewardship.
- Restricted antimicrobials were defined based on the hospital's antibiogram data, which identified them as last-resort agents for treating multidrug-resistant organisms, and included carbapenems (meropenem, ertapenem, and imipenem), polymyxins (B and E), glycopeptides (teicoplanin and vancomycin), cephalosporins (ceftazidime/avibactam and ceftaroline), linezolid, fosfomycin, tigecycline, and antifungals (caspofungin, anidulafungin, micafungin, and amphotericin B).
- During the intervention period, clinical pharmacists extracted a list every day of patients who had been prescribed a restricted antimicrobial the previous day from the pharmacy database, along with information on the admission date, prescribed antimicrobial, and hospital location.
- Clinical pharmacists documented the proposed intervention and their acceptance or rejection reason, but the intervention was not documented in the medical record.
- Patients were continuously monitored until discharge, and their clinical and demographic data were extracted from the medical record.

- Antimicrobial consumption data, expressed as average daily defined dose (DDD) per 1,000 inpatient days, were collected from the pharmacy database.[i]

Study Population

- During the intervention phase, 17,178 patients were admitted to the facility and 8,722 of them received at least one antimicrobial therapy. Of these, 1,096 patients (mean age 57.9 [standard deviation (SD) 17.1], 62% male) received restricted antimicrobials and underwent review by the clinical pharmacists.
- During the pre-intervention phase, 1,228 patients (mean age 56.9 [SD 16.6], 62% male) received restricted antimicrobials.
- The most common primary sources of infection were:
    - Urinary tract infection (23% pre-intervention vs. 30% intervention, p=0.04)
    - Respiratory tract infection (20% pre-intervention vs. 21% intervention, p=0.58)
    - Bloodstream infection (14% pre-intervention vs. 17% intervention, p=0.24)
    - Intra-abdominal infection (19% pre-intervention vs. 14% intervention, p<0.001)
- In the intervention period, patients receiving restricted antimicrobials were most commonly admitted to general medicine (25.5%) or orthopedics (15.1%).

Clinical Pharmacist Interventions

- During the intervention phase, a total of 609 interventions were proposed, of which 485 (79.6%) were accepted.
- Of the accepted interventions, 417 (85.9%) pertained to intravenous antimicrobial therapy, while the remaining 68 (14.1%) were for oral formulations.
- The most common interventions proposed were:
    - De-escalation or discontinuation for excessive duration (N=210, 85% accepted)
    - De-escalation based on culture reports (N=140, 75% accepted)
    - Dose adjustment as per standard guidelines (N=89, 88% accepted)
    - Dosage or frequency adjustment as per creatinine clearance and augmented renal clearance (N=56, 89% accepted)
- Over time, both the frequency and rate of intervention acceptance increased, from 55.6% (15/27) in April 2022 to 96.3% (78/81) in March 2023.

Antimicrobial Consumption

- The total number of inpatient days during the pre-intervention and intervention periods were 64,490 and 67,226, respectively (p = 0.47).
- There was a reduction in the daily defined dose (DDD) per 1,000 inpatient days in the intervention phase compared to the pre-intervention phase for polymyxins (58% [SD 3.04 to 1.29]), carbapenems (7% [SD 57.09 to 52.85]), and glycopeptides (10% [SD 47.44

to 42.73]), although none of these changes were statistically significant. The reduction in DDD in these three classes combined was statistically significant (p=0.04, 95% confidence interval [CI]=0.3–7.0).

- There was an increase in the consumption of cefoperazone/sulbactam (16% [SD 73.50 to 84.90]) and piperacillin/tazobactam (1% [SD 47.7 to 48]), which are unrestricted antimicrobials that are commonly used as alternatives to carbapenems and have a narrower spectrum of activity.

Critical Analysis

This single-center quasi-experimental study demonstrated that clinician training as part of an antimicrobial stewardship program resulted in increased acceptance of interventions recommended by clinical pharmacists using the prospective audit and feedback approach. The study also found that implementation of the antimicrobial stewardship program resulted in a decrease in consumption of restricted antimicrobials compared to the pre-intervention period.

The following points should be considered when interpreting the study findings:

- The study did not take into consideration antimicrobial de-escalation made by the infectious disease physician as a part of routine individual practice, which may have confounded the observed association between implementation of prospective audit and feedback by clinical pharmacists and antimicrobial de-escalation. However, an infectious diseases physician was present at the hospital in both the pre-intervention and intervention periods.
- An analysis of the correlation between decreased consumption of restricted antimicrobial agents and changes in the prevalence of resistant strains in the hospital setting was not conducted. This is a long-term goal of antimicrobial stewardship programs which may not be realized after one year of implementation.
- The study utilized DDDs instead of days of therapy. Antimicrobial utilization data presented in DDDs only provide a rough estimate of consumption, and do not represent actual use. DDDs do, however, allow for comparison across facilities, and are more feasible to measure in resource-constrained healthcare settings.
- Clinical outcomes such as hospital length of stay, mortality rates, and unintended consequences such as *Clostridium difficile* infection are important indicators of antimicrobial stewardship program effectiveness, however these data were not reported.
- The assessment was conducted in a single hospital, and the findings may not be generalizable to health facilities with different contextual characteristics.

Implications

This single-center quasi-experimental study demonstrated that clinical pharmacists can play a vital role in implementing an antimicrobial stewardship program in tertiary care hospitals.

Clinician education, coupled with prospective audit and feedback, can lead to a more rational use of antimicrobials and meaningful reductions in the consumption of restricted antimicrobials.

This article synopsis was written by Dr. Getachew Kassa. Share your thoughts on this article or suggest an article for Journal Club by emailing him at gk2353@cumc.columbia.edu.

[i] World Health Organization. Defined Daily Dose. Available from: https:// www.who.int/tools/atc-ddd-toolkit/about-ddd