31. Stepwise Expansion of Antimicrobial Stewardship Program and Its Impact on Antibiotic Use and Resistance Rates in a Tertiary Care Hospital in Korea

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Session: P-04. Antimicrobial Stewardship: Outcomes Assessment (clinical and economic)

Background. The U.S. Centers for Disease Control and Prevention released the core elements of antimicrobial stewardship program (ASP). In some countries, however, they may be difficult to apply in countries with limited resources. In this study, we evaluated the impact of successful ASP implementation on antibiotic use and resistance rates in an institution with limited infrastructural support.

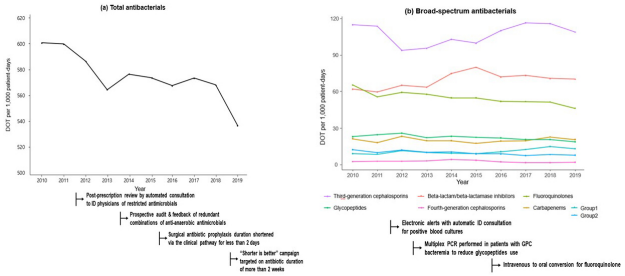
Methods. A series of ASP activities were reviewed according to the core elements of ASP. The retrospective data of all hospitalized patients at a tertiary care teaching hospital was collected from January 2010 to December 2019, including antibiotic prescription data and culture results of all clinical specimens. The trends of the antibiotic-resistant rates were compared with nationwide data in Korea. The trend analyses were performed with 2-sided correlated seasonal Mann-Kendall nonparametric tests.

Results. The ASP activities over the past decade were summarized in Table. After activities such as preauthorization were achieved, other ASP activities were added one by one. Also, the infectious disease pharmacists, as ASP co-leaders, mainly carried out the following activities: reducing redundant anti-anaerobic antimicrobials and intravenous fluoroquinolones, and advised the physicians to discontinue the antibiotic prescription in cases when the intervention was plausible. After the ASP implementation, total antibacterial use significantly decreased ($P < 0.01$; Figure). The use of glycopeptides ($P < 0.01$) and fluoroquinolones ($P < 0.01$) gradually decreased, while the use of third-generation cephalosporines did not significantly change (P=0.48). There was no significant change in total carbapenems use, but ertapenem use increased (P=0.02). Compared with the nationwide data, methicillin-resistant *Staphylococcus aureus* was on a decreasing trend consistently. Although third-generation cephalosporin-resistant *Escherichia coli* increased, third-generation cephalosporin resistant-*Klebsiella pneumoniae* and carbapenem resistant-*Pseudomonas aeruginosa* did not increase.

Table. Antimicrobial stewardship activities for hospitalized patients over the past decade in Seoul National University Bundang Hospital. ASP: antimicrobial stewardship; ID: infectious disease; CDSS: Clinical decision support system

ASP core elements	Examples	Starting point
Hospital leadership	**Staffing**, partly involved in ASP activities • 4 ID (3 adult and 1 pediatric) physicians at a hospital expanded to over 1,300 beds	March 2011
	Pharmacy & therapeutics committee • Promoted to ASP committee • Established a new subcommittee for therapeutic drug monitoring of antibiotics	November 2018 September 2019
Accountability	• An ASP team consisting of ID specialists, pharmacists, and microbiology laboratory staffs	November 2018
Pharmacy expertise	• ID training for the pharmacists • 1 full-time ID pharmacist designated for ASP	March 2013 May 2019
Action	**Preauthorization** • Post-prescription review and feedback of restricted antimicrobial by automated consultation to ID physicians	August 2011
	Prospective audit & feedback • Electronic alerts with automatic ID consultation for positive blood cultures • Redundant combinations of metronidazole or clindamycin with other anti-anaerobic antimicrobials • Intravenous to oral conversion for fluoroquinolone and metronidazole • "Shorter is better" campaign targeted on antibiotic duration of more than 2 weeks	August 2011 July 2013 August 2015 August 2018
	Facility-specific treatment guidelines • For surgical antibiotic prophylaxis, the duration shortened via the clinical pathway - less than 2 days - less than 24 hours	 April 2015 April 2020
	Pharmacologic intervention • Vancomycin loading by the computerized CDSS • Daily alerts using ASP review sheet specialized for the pharmacists on electronic medical record - intravenous to oral conversion - inappropriate dosing according to indications and renal function - drug interactions and adverse events	July 2016 November 2016
	Rapid diagnostics • Multiplex polymerase chain reaction performed in patients with gram-positive cocci in clusters bacteremia	February 2012
Tracking	**Antibiotic use measures** • Monitoring antibiotic administration data from clinical data warehouse (defined daily dose, day of therapy, and length of therapy per 1,000 patient-days)	July 2014
	Outcome measures • Weekly meeting with the microbiology laboratory as well as the infection control office • Daily morning conference with the pharmacists	March 2017 March 2013
Reporting	• Regular report on the proportion of clinical consultations on therapeutic drug monitoring services of antibiotics administered for over 7 days	December 2019
Education	• Education programs for not only physician but also pharmacists • Educational material development by elective course internal medicine residents, and then shared with other physicians	March 2016 March 2016

Figure. DOT per 1,000 patient-days in Seoul National University Bundang Hospital and implemented actions of antimicrobial stewardship program. DOT: days of therapy; ID: infectious disease; PCR: polymerase chain reaction; GPC: gram positive cocci; Group 1 carbapenem: ertapenem



Conclusion. A stepwise implementation of the core ASP elements was effective in improving the appropriate use of antibiotics and reducing the antibiotic resistant organisms, even with limited human resources.

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32. Impact of a Four-Year Antimicrobial Stewardship Program on Antimicrobial Resistance

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Session: P-04. Antimicrobial Stewardship: Outcomes Assessment (clinical and economic)

Background. Antimicrobial resistance (AMR) is an increasing threat to public health and antimicrobial consumption is a primary driver of resistance. Many studies have shown that the implementation of an antibiotic stewardship program (ASP) improves prescribing of antibiotics and can reduce AMR. Purpose of the study was to assess the impact of a successful ASP, implemented for four years, on AMR in our 427-bed tertiary general hospital.

Methods. We monitored pharmacy data for the years 2015 (pre-intervention) and 2016-2019 (post-intervention) for antibiotic consumption (DDD/100 bed-days) and resistance rates. AMR data were obtained from the clinical microbiology laboratory's electronic database. To achieve the goals of ASP we used a range of interventions as pre-authorization strategy for the protected antibiotics (tigecycline, carbapenems, quinolones, glycopeptides, daptomycin, colistin, linezolid), prospective audit and feedback with direct intervention, de-escalation or switch from iv to oral administration and appropriate selection and duration of chemoprophylaxis in surgery.

Results. Significant reductions were observed for: total antibiotics, colistin, carbapenems, quinolones and tigecycline consumption during study period. Significantly lower resistance rates were documented in 2019 compared to 2015 for *Pseudomonas aeruginosa* and for *Klebsiella pneumoniae*. As for *Acinetobacter baumannii* isolates, which in our hospital are highly-resistant exhibiting >90% resistance to carbapenems, no significant changes were noted during the study period. Infections caused by Gram-positive pathogens are less prevalent in our hospital. Lower rates of vancomycin-resistant enterococci were noted after the implementation of our ASP (30.4% in 2019 vs. 50.0% in 2015 for *E. faecium* and 0.6% vs. 6% for *E. faecalis*, respectively), whereas methicillin-resistant *S. aureus* isolates increased (40% in 2019 vs. 31.1% in 2015), possibly because most of these infections were not hospital-acquired.

Resistance rates of Pseudomonas and Klebsiella

Resistance rates (%) for *P. aeruginosa*						
	2015	2016	2017	2018	2019	P
AMIKACIN	46	51	34.4	33.2	15.6	<0.0001
CIPROFLOXACIN	53	59	41.3	51	24.9	0.0003
CEFTAZIDIME	55	61	23.4	28.9	13.2	<0.0001
CEFEPIME	49	54	30.7	28.8	13.4	<0.0001
PIP/TAZO	52	49	23.3	20.3	9.8	<0.0001
MEROPENEM	57	63	37.2	42.7	22.6	<0.0001
IMIPENEM	61	71	38.8	47.2	25.2	<0.0001
COLISTIN	7	7	0.0	0.3	0.3	0.0001
Resistance rates (%) for *K. pneumoniae*						
	2015	2016	2017	2018	2019	P
AMIKACIN	55.4	31.5	31.3	44.9	27.2	<0.0001
CIPROFLOXACIN	81.1	82.3	73.8	68.1	70.1	0.518
CEFOTAXIME	81.8	84.0	71.6	67.9	67.7	0.0665
CEFEPIME	83.5	75.5	68.0	64.0	62.7	0.0061
PIP/TAZO	81.8	86.2	69.3	62.1	65.8	0.0061
MEROPENEM	81.2	85.6	66.3	59.7	61.8	0.0087
IMIPENEM	76.5	81.8	65.1	59.6	62.2	0.0519
TIGECYCLINE	26.4	16.2	3.9	8.3	19.2	0.1855
COLISTIN	48.9	27.9	17.8	6.7	9.3	<0.0001