

급성 상기도 감염에서 항생제 처방개선에 관한 연구

강혜경

경상대학교병원 약제부, 경상대학교 식의약품대학원

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Efforts to Improve Antibiotic Prescribing Trends for Acute Upper Respiratory Infections in a South Korean University Hospital

Hyekyung Kang

Department of Pharmacy, Gyeongsang National University Hospital; Graduate School of Food and Drug Administration, Gyeongsang National University, Jinju, Republic of Korea

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목적: 급성 상기도 감염에 사용되는 항생제 처방유형을 조사하여 항생제 사용을 개선하는데 있다.

방법: 2011년 1월부터 6월까지 경상대학교 병원을 포함한 10개 국립대학병원을 대상으로 급성 상기도 감염에 사용한 항생제 처방율을 조사하고, 경상대학교병원에서 급성 상기도 감염에 사용한 2011년 1월부터 6월까지의 외래환자를 대상으로 항생제 처방 내역을 전자의무기록을 통하여 후향적으로 분석한 후 처방의를 대상으로 항생제 사용 적정성 검토를 위한 그룹핑 및 교육, 급성 상기도 감염에 항생제 처방 시 경고 안내문을 보여주는 등 중재활동 후 2011년 12월에 처방유형을 조사 하였다.

결과: 경상대학교병원에서 2011년 1월부터 6월까지 급성 상기도 감염에 항생제 사용은 1739명의 상기도 감염 외래 환자 중에서 874명 (42.3%)으로 나타났다. 진료과별 급성 상기도 감염에 대한 항생제 처방은 소아과, 이비인후과, 내과, 응급의학과, 호흡기내과, 흉부외과 등에서 처방하였으며 소아과에서 1044명의 상기도 감염환자 중 556건 (53.3%)로 가장 빈번하게 사용하였으며 처방율은 이비인후과에서 58.9% (225/382)로 가장 높았다. 사용한 항생제로는 amoxicillin-clavulanic acid가 371례 (36.3%)로 가장 빈번하게 처방된 약제이며, azithromycin이 85례 (9.7%) 처방되었다. 급성 상기도 감염 중 급성 편도염에 항생제 처방율이 가장 높았으며 (70.8%, 80/113), 급성 인두염에 가장 빈번하게 사용되었다 (61.1%, 319/522). 균동정을 위한 혈액배양 의뢰 건수는 1739 상기도 감염 환자 중 15명 (항생제 미사용 4명, 사용 11명)이 의뢰되었으며 모두 음성이었다. 중재활동 후 2011년 12월 상기도 감염에 항생제 처방건수는 소아과에서 1건, 이비인후과에서 2건으로 나타났다.

결론: 처방의를 대상으로 적절한 항생제를 사용을 권장하는 지속적인 교육 및 항생제 처방시 경고 안내문을 띄우는 등의 중재활동과 지속적인 모니터링 및 피드백은 급성 상기도 감염에 있어서 항생제 처방유형에 변화를 보였다.

□ Key words - acute upper respiratory infections (AURIs), antibiotic prescribing trends, interventions

INTRODUCTION

Antimicrobial resistance promoted by appropriate and inappropriate use of antibiotics has been a growing concern for health care professionals. Physicians often prescribe antibiotics for patients, although these prescriptions

may have uncertain results. Acute upper respiratory infections (AURIs) are one of the common reasons for antibiotic use despite the finding that most AURIs are viral and do not respond favorably to antibiotic therapy.^{1,2)} It has been reported that excessive use of broad-spectrum antibiotics can cause viral illnesses.³⁾ Inappropriate antibiotic use increases antimicrobial resistance and overall health care costs.

Antibiotic-resistant strains of common pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus* are emerging at alarming rates, and the excessive use of inappropriate antimicrobial

Correspondence to : Hyekyung Kang

Department of Pharmacy, Gyeongsang National University Hospital; Graduate School of Food and Drug Administration, Gyeongsang National University, Jinju, Republic of Korea
Tel: +82-55-750-8008, Fax: +82-55-750-8627
E-mail: neulsaem@gnu.ac.kr

agents aggravates this problem.^{4,5)} The increase in drug resistance by excessive use of antibiotics has resulted in more expensive treatment alternatives. Patients infected with drug-resistant organisms have had to be hospitalized for longer durations.⁶⁾

Antimicrobial agents comprised 12% to 14% of all drugs prescribed in the United States, and AURIs were one of the common causes for antibiotic use, accounting for about 20% of all antibiotics prescribed.⁷⁾ Given the growing concern over antimicrobial resistance, some studies suggest that regardless of duration, antibiotic treatment of patients with AURIs does not improve illness resolution and is not recommended.⁸⁻¹⁰⁾ In Gyeongsang National University Hospital (GNUH), antimicrobial agents have been the most common category of medications prescribed (15%).

The objective of this study was to improve trends in antibiotic prescribing for acute upper respiratory infections (AURIs) in a South Korean university hospital by performing interventions. A comprehensive analysis of antibiotic prescribing rates for patients with diagnoses of AURIs in 10 national university hospitals in South Korea including GNUH from January to June 2011 was obtained from Health Insurance Review and Assessment Service (HIRA). The efforts to reduce antibiotic prescription rates for AURIs were evaluated in December 2011 by comparing prescribing activity before and after implementation of the interventions at GNUH.

METHODS

Patients and sources of information

This study identified 874 outpatients who were prescribed antibiotics after being diagnosed with AURIs at GNUH. The total number of outpatients who were diagnosed with AURIs at GNUH during the study's time-frame from January to June 2011 was 1739. A total of 1739 outpatients were diagnosed with AURIs at GNUH between January and June 2011. Outpatient visits included single or multiple hospital visits resulting in a primary diagnosis of AURIs by the Korean Standard Classification of Diseases, 6th revision (KCD-6). This

study identified 874 outpatients who were prescribed antibiotics after being diagnosed with AURIs.

The study was conducted at GNUH in South Korea, a 910-bed tertiary care hospital that is comprised of 30 units including but not limited to pediatrics, ENT, internal medicine, respiratory medicine, gastrointestinal medicine, and emergency medicine for inpatient and outpatient services.

This research evaluated antibiotic prescription rates for AURIs from January to June 2011 at 10 national university hospitals including GNUH. The data were obtained from the Health Insurance Review and Assessment Service (HIRA, http://www.hira.or.kr/rec_infopub_hosp_info.do?method). At GNUH, a retrospective study was conducted using Electronic Medical Records (EMR) to assess antibiotic prescriptions for AURIs from January to June 2011 and to compare the prescription rates before and after the interventions in December 2011.

Korean Standard Classification of Diseases, 6th revision (KCD-6) was used to identify AURIs. The AURIs included acute nasopharyngitis (KCD-6 code J00), acute sinusitis (KCD-6 code J01), acute pharyngitis (KCD-6 code J02), acute tonsillitis (KCD-6 code J03), acute laryngitis and tracheitis (KCD-6 code J04), acute obstructive laryngitis and epiglottitis (KCD-6 code J05), and acute upper respiratory infections of multiple or unspecified sites (KCD-6 code J06). Patients diagnosed with chronic obstructive pulmonary disease (COPD), chronic bronchitis, and chronic diseases such as emphysema and asthma were excluded. Patients with multiple diagnoses were documented under the primary disease.

Antibiotic use by specialties

Antibiotic prescriptions were identified using both trade and generic names. Antibiotic classes included in this study were penicillins, cephalosporins, quinolones, macrolides (including azalides), lincosamides, and sulfonamides. The prescriptions of more than two antibiotic classes for one observation were documented to each class. Antibiotic use for AURIs from January to June 2011 at GNUH was evaluated to identify specialty

variations. All specialties-used antibiotics for AURIs such as pediatrics, ENT, internal medicine, respiratory medicine, gastrointestinal medicine, cardiothoracic surgery, and emergency medicine were included in this study; however, the specialties-rarely-used antibiotics for AURIs were classified as “others.” The data used to measure antibiotics prescribed and design appropriate interventions were analyzed by percentage rates rounded to the nearest tenth.

Interventions

Group education meetings

Special group education meetings were launched with the purpose of improving antibiotic prescribing behaviors for AURIs. In these weekly meetings held throughout November 2011, physicians, administrative assistants, and a pharmacist discussed the HIRA data that identified inappropriate antibiotics use and provided an overview of evidence-based antibiotic use with culture results. Diagnostic categories of AURIs identified by KCD-6 included acute nasopharyngitis, acute sinusitis, acute pharyngitis, acute tonsillitis, acute laryngitis and tracheitis, acute obstructive laryngitis and epiglottitis, and acute upper respiratory infections of multiple or unspecified sites. The intensive group education meetings resulted in the hospital creating a consensus on the restricted use of antibiotics in the treatment of AURIs.

Launching an Alarm System for Prescribers through the EMR System

Beginning in December 2011, antibiotic prescriptions for AURIs in all specialties were blocked completely in the EMR unless specific reasons for antibiotic prescribing were properly documented. The alarm system through the EMR warned prescribers about antibiotics use for AURIs patients. The pop-up window with warning comments against antibiotics use for AURIs appeared when prescribers tried to prescribe antibiotics to patients with AURIs identified by KCD-6 (Figure 1). The antibiotic use for AURIs in pediatrics was highly restricted.

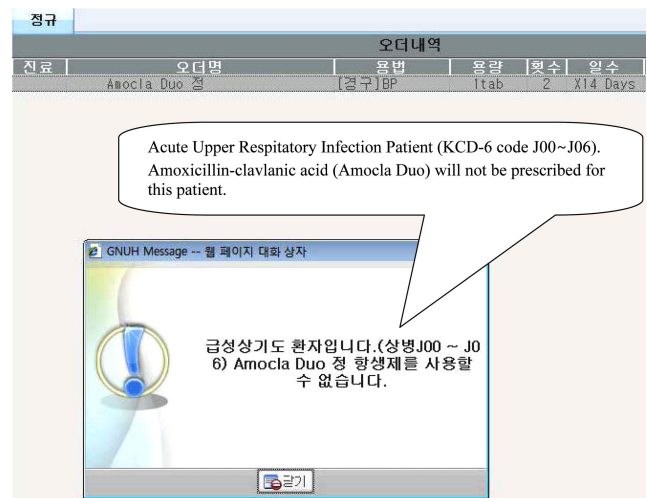


Fig. 1. Pop-up window warning prescribers of prescribing antibiotics for AURIs.

Monitoring and feedback on prescribing behavior

In addition to group education meetings and launching an alarm system for prescribers through the EMR system, monitoring efforts and feedback platforms on prescribing behaviors were established to reduce the number of antibiotics prescriptions in December 2011 at GNUH.

RESULTS

There were 874 (50.3%) antibiotic prescriptions for 1739 patients diagnosed with AURIs at GNUH from January to June 2011. The largest age group for AURIs visits was between the ages of 0 and 17. Antibiotics were prescribed in 588 cases (53.8%) out of the 1093 patients comprising this age group. The most frequent use of antibiotics for AURIs was in pediatrics with 556 prescriptions (53.3%) out of 1044 visits. The highest antibiotic prescription rate was in ENT with 225 prescriptions (58.9%) out of 382 visits. Acute tonsillitis (KCD-6 code J03) showed the highest antibiotic prescription rate with 80 prescriptions (70.8%) out of 113 visits. Antibiotics were most frequently prescribed for acute pharyngitis (KCD-6 code J02) with 319 prescriptions (61.1%) out of 522 visits. Fifteen patients (4 cases without antibiotics use and 11 cases with

Table 1. Characteristics of 1739 patients with AURIs visits from January to June 2011 at GNUH

	No antibiotics Rx N=865 (4)	Antibiotics Rx (A) N=874 (11)	Total (B) N=1,739 (15)	A/B*100 %
Sex				
Male	415 (1)	418 (4)	833 (5)	50.2
Female	450 (3)	456 (7)	906 (10)	50.3
Age				
0-17	505 (3)	588 (6)	1,093 (9)	53.8
18-44	153	160 (5)	313 (5)	51.1
45-64	150 (1)	94	244 (1)	38.5
65<	57	32	89	36.0
Specialty				
Pediatrics	488 (3)	556 (6)	1,044 (9)	53.3
ENT	157	225 (1)	382 (1)	58.9
Internal medicine	105 (1)	56 (3)	161 (4)	34.8
Emergency medicine	6	16 (1)	22 (1)	72.7
Respiratory medicine	31	6	37	16.2
Cardiothoracic surgery	26	3	29	10.3
Gastrointestinal medicine	8	2	10	20.0
Others	44	10	54	18.5
Diagnosis				
Acute nasopharyngitis	312 (1)	134 (3)	446 (4)	30.0
Acute sinusitis	84	176 (2)	260 (2)	67.7
Acute pharyngitis	203	319 (3)	522 (3)	61.1
Acute tonsillitis	33	80	113	70.8
Acute laryngitis and tracheitis	27	7	34	20.6
Acute obstructive laryngitis and epiglottitis	16	10	26	38.5
Acute URIs of multiple and unspecified sites	190 (3)	148 (3)	338 (6)	43.8

() number of culture order

antibiotics use) out of 1739 AURIs patients were asked for microbial blood cultures. All showed negative results. In addition, results related to antibiotic prescribing for AURIs did not differ by gender (Table 1).

According to the Health Insurance Review and Assessment Service (HIRA), from January to June 2011 GNUH showed the second highest antibiotic prescription rate for AURIs at 42.3% among 10 South Korean university hospitals. The highest rate was 42.6% at Kangwon National University Hospital. Ratings for the other South Korean university hospitals are as follows: 37.2% at Chonbuk National University Hospital, 36.4% at Chonnam National University Hospital, 31.9% at Chungnam National University Hospital, 29.0% at Chungbuk National University Hospital, 27.5% at Jeju National University Hospital, 26.6% at Pusan National

University Hospital, 15.8% at Seoul National University Hospital, and 0.5% at Kyungpook National University Hospital (Figure 2).

Among the antibiotic classes, penicillins were prescribed the most frequently for AURIs from January to June 2011 at GNUH. The percentage of penicillins prescribed for AURIs was 38.6%, followed by cephalosporins (33.3%), macrolides (20.0%), sulfonamides (5.3%), quinolones (2.7%), and lincosamides (0.1%). Among all antibiotics used in the treatment of AURIs, amoxicillin-clavulanic acid was the most frequently prescribed with 317 cases (36.3%) among 874 total antibiotics used. The second most frequently prescribed antibiotic was azithromycin in 85 cases (9.7%). Antibiotics use among medical specialties varied. Antibiotics were prescribed the most in pediatrics (63.6%, 556 out

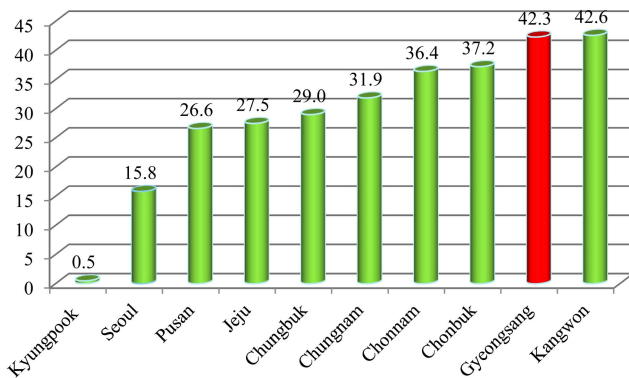


Fig. 2. Antibiotic prescription rates for AURIs from January to June 2011 in 10 national university hospitals.

of 874 cases). Pediatrics was followed by ENT (25.7%, 225 out of 874 cases), internal medicine (6.4%, 56 out of 874 cases), emergency medicine (1.8%, 16 out of 874 cases), respiratory medicine (0.7%, 6 out of 874 cases), cardiothoracic surgery (0.4%, 3 out of 874 cases), gastrointestinal medicine (0.2%, 2 out of 874 cases), and others (1.2%). Regarding specialties-used antibiotics for AURIs, penicillins, including amoxicilline-clavulanic acid, were prescribed the most frequently (218 times), followed by macrolides (155 times) and sulfonamides (46 times) in pediatrics. In ENT, chephalosporins were the most frequently prescribed (140 times), followed by

Table 2. Antibiotics use for AURIs by specialties from January to June 2011 at GNUH

Antibiotics	PD N=556 (63.6)	ENT N=225 (25.7)	IM N=56 (6.4)	EM N=16 (1.8)	IP N=6 (0.7)	CS N=3 (0.4)	IG N=2 (0.2)	Others N=10 (1.2)	Total N=874 (%)
Penicillins	218	70	29	10		3	1	6	337 (38.6)
Amoxicillin	16	2				1			19 (2.2)
Amoxicillin / Clavulanate	202	68	29	10		1	1	6	317 (36.3)
Ampicillin						1			1 (0.1)
Cephalosporins	136	140	13	1				1	291 (33.3)
Cefaclor			1	1					2 (0.2)
Cefcapene		52							52 (5.9)
Cefdinir	48	12							60 (6.9)
Cefditoren	2	34							36 (4.1)
Cefixime	52	5	1						58 (6.6)
Cefotaxime	2								2 (0.2)
Cefpodoxime	28	33	11					1	73 (8.4)
Ceftriaxone	3								3 (0.3)
Cefuroxime		4							4 (0.5)
Cephadroxil	1								1 (0.1)
Macrolides	155	3	5	4	5		1	2	175 (20.0)
Azithromycin	75		5	2			1	2	85 (9.7)
Clarithromycin	18								18 (2.1)
Erythromycin					1				1 (0.1)
Roxithromycin	62	3		2	4				71 (8.1)
Sulfonamides	46								46 (5.3)
TMS/SMX	46								46 (5.3)
Quinolones		12	9	1	1			1	24 (2.7)
Ciprofloxacin		7	1	1					9 (1.0)
Gemifloxacin		5	1		1				7 (0.8)
Levofloxacin			5						5 (0.6)
Mocifloxacin			2					1	3 (0.3)
Lincosamides	1								1 (0.1)
Clindamycin	1								1 (0.1)

PD: Pediatrics, ENT: Otolaryngology (ear, nose and throat), IM: Internal medicine, EM: Emergency medicine, IP: Respiratory medicine, CS: Cardiothoracic surgery, IG: Gastrointestinal medicine

Table 3. Antibiotic classes prescribed for AURIs by age and diagnosis from January to June 2011 at GNUH

	Penicill N=337	Cepha N=291	Macrol N=175	Sulfona N=46	Quinol N=24	Lincos N=1	Total N=874
Age							
0-17	227	156	158	46		1	588
18-44	75	70	4		11		160
45-64	27	45	13		9		94
65<	8	20			4		32
Diagnosis							
Acute nasopharyngitis	46	34	33	12	9		134
Acute sinusitis	33	87	33	15	8		176
Acute pharyngitis	154	80	71	10	3	1	319
Acute tonsillitis	39	32	7	2			80
Acute laryngitis and tracheitis	3	4					7
Acute obstructive laryngitis and epiglottitis		9	1				10
Acute URIs of multiple and unspecified sites	62	45	30	7	4		148

Penicill: Penicillins, **Cepha:** Cephalosporins, **Macrol:** Macrolides, **Sulfona:** Sulfonamides **Quinol:** Quinolones, **Lincosa:** Lincosamides

penicillines (70 times) (Table 2).

Among diagnoses of AURIs including acute nasopharyngitis (J00), acute sinusitis (J01), acute pharyngitis (J02), acute tonsillitis (J03), acute laryngitis and tracheitis (J04), acute obstructive laryngitis and epiglottitis (J05), and acute upper respiratory infections of multiple or unspecified sites (J06), the most frequent visits (319 out of 874) involved acute pharyngitis (J02). Among the 319 visits with acute pharyngitis (J02), penicillins were prescribed 154 times. Also, penicillines were the most frequently prescribed antibiotics for the age group between the ages of 0 and 17 (Table 3).

After the interventions including group education meetings, launching an alarm system for prescribers through the EMR system, and monitoring and feedback on prescribing behavior, the overall numbers of prescriptions with AURIs were 3 cases; 1 case in pediatrics, 2 cases in ENT by December 2011.

DISCUSSION

There has been no conclusive evidence indicating that antibiotics have a clinical benefit for patients with AURIs; however, the antibiotic prescribing rates for AURIs continue to remain high. Most antibiotics prescribed for AURIs present little to no benefits for the

patient, and antimicrobial resistance due to either appropriate or inappropriate use of antibiotics has become a public health problem.^{11, 12)} The emergence of drug resistance has been closely related to antibiotic use.^{13, 14)} Incidents of adverse effects by use of antibiotics and financial considerations regarding unnecessary medical visits are of further concern.^{15, 16)}

Previous studies have shown that physicians overprescribe antibiotics to patients without appropriate considerations.^{17, 18)} Studies abroad have also found that up to 75% of patients with acute bronchitis receive antibiotics without evidence or benefit, and up to 60% of patients with upper respiratory infections or colds that were prescribed antibiotics showed no improvement of outcomes.¹⁹⁻²¹⁾ However, in previous studies, efforts to reduce antibiotic use have improved in antimicrobial prescribing rates for upper respiratory tract infections.^{22, 23)}

In this study, from January to June 2011 and among 10 national university hospitals, GNUH showed the second highest antibiotic prescription rates for AURIs (42.3%). It was determined that the efforts to reduce antibiotic prescription rates for AURIs were necessary as compared with other university hospitals: Chonbuk National University Hospital (37.2%), Chonnam National University Hospital (36.4%), Chungnam National University Hospital

(31.9%), Chungbuk National University Hospital (29.0%), Jeju National University Hospital (27.5%), Pusan National University Hospital (26.6%), Seoul National University Hospital (15.8%), and Kyungpook National University Hospital (0.5%). Kyungpook National University Hospital showed the lowest antibiotic prescription rates for AURIs (0.5%) due to their successful intervention in blocking antibiotic prescriptions for inappropriate indications.

At GNUH, antibiotic use for AURIs among medical specialties varied, and pediatrics showed the most frequent use (53.3%) from January to June 2011. The increased use in pediatrics was driven by a greater number of prescriptions for amoxicillin-clavulanic acid and azithromycin. The study identified 15 patients out of 1739 who were asked for microbial blood cultures. All fifteen cases (11 cases including antibiotics use and 4 cases not including antibiotics use) produced negative results. This may be a consequence of the prescribers' reactions to increasing beta-lactam resistance to common pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*.^{4,5)} The increased use of amoxicillin-clavulanic acid and azithromycin could also be related to increased compliance with simple dosing instructions for these antibiotics. However, broad-spectrum antibiotics provide minimal clinical advantage over narrow-spectrum agents or no antibiotic therapy in non-pneumonic AURIs.^{9,10)}

The overall numbers of prescriptions with AURIs were 3 cases; 1 case in pediatrics, 2 cases in ENT by December 2011 after by blocking prescriptions unless prescribers documented specific reasons for antibiotic usage. The interventions of group educational meetings, blocking or alarming against antibiotic prescriptions for AURIs through the EMR system, and monitoring and feedback on prescribing behavior helped prescribers to significantly change their antibiotic prescribing behaviors. Gaining consensus on the restricted use of antibiotics in the treatment of AURIs through the group education meetings in the hospital was supportive to improve antibiotic prescribing behaviors.

There were limitations to this study. First, antibiotic prescriptions were documented, but medication compli-

ance was not able to be determined. Second, this study was retrospective using administrative databases with limitations including coding errors. However, these databases may be allowed for analysis on AURIs antibiotic prescribing rates in this study.

In conclusion, continued education directed at specific specialties in proper antibiotic use is needed to improve antibiotic prescribing behaviors. Blocking and alarming systems against antibiotic use may be one of the most effective ways to improve proper antibiotic use. Continuous monitoring and feedback on prescribing behavior are necessary to reduce antibiotic prescription rates for AURIs.

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