# International initiatives to control antimicrobial resistance : I Care project

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## I. Introduction

Antimicrobial resistance in major bacterial pathogens is a global healthcare threat that can seriously jeopardize the public health worldwide. Most of the important bacterial pathogens have developed antimicrobial resistance to major antimicrobial options. Clinical and economic impact of antimicrobial resistance is devastating, especially in developing countries. Among many factors that can affect the emergence and spread of antimicrobial resistance, antimicrobial abuse or misuse is the most important and a basic driving force to induce the resistance. In the clinical practice, abuse or misuse of antibiotics may not result in immediate harm or problems to the patients. Therefore, antibiotics are the most common drugs to be used inappropriately and unreasonably. Inappropriate use of antimicrobial agents is a worldwide problem that can induce the emergence of antimicrobial resistance and increase the healthcare cost, although developing countries have more serious problems of drug abuse. In many developing countries, antibiotics are among the most frequently used therapeutic agents. For instance, antibiotics take first place among all drugs used in Turkey with 22 %[1]. Given the importance of antimicrobial uses for the emergence of antimicrobial resistance, strategies to control and prevent this problem should be based on appropriate use of antimicrobial agents.

## II. Factors affecting the emergence of antimicrobial resistance

There are many factors that can affect the emergence of antimicrobial resistance in major bacterial pathogens. The most important driving force for the emergence of resistance is antibiotic consumption, especially antibiotic abuse or misuse. Relationship between antibiotic uses and antimicrobial resistance is quite obvious as documented in many papers. Inappropriate use of antimicrobial agents is due to many reasons including unnecessary use of antibacterial agents, especially in viral infections, wrong selection of antibiotics, and wrong doses or duration. Counterfeit drugs that contain inadequate amount of antimicrobial compounds are another form of antibiotic misuse, which is a serious problem in developing countries. Secondly, the spread of resistant clones or genes is important to increase the prevalence of antimicrobial resistance during a short period. It occurs between the regions and countries, which makes antimicrobial resistance an international issue. Other factors include social factors and microbial factors such as specific serotypes or microbial characteristics.

## III. Relationship between antimicrobial uses and antimicrobial resistance

### 1. Increased use of antibiotics vs increased antimicrobial resistance

Increased use of antibiotics is the main selective pressure for the emergence of antimicrobial resistance in major bacterial pathogens. There have been many data that documented the impact of increasing consumption of antibiotics on the prevalence of antimicrobial resistance. According to the multinational surveillance in Europe by ESAC Project Group, higher rates of antimicrobial resistance were noted in high consuming countries, probably related to the higher consumption in southern and eastern Europe than in northern Europe. Data showed a strong correlation between penicillin use and the prevalence of penicillin-non-susceptible *S. pneumoniae* in European countries[2]. Data from Taiwan also showed that increase in cefotaxime-resistant or ciprofloxacin-resistant *E.coli* and meropenem-resistant *P. aeruginosa* was significantly correlated with increased consumption of extended-spectrum cephalosporins, β-lactam-β-lactamase inhibitor combinations, carbapenems, fluoroquinolones and aminoglycosides in the hospital. This study clearly documented significant correlations between antimicrobial use and the prevalence of antimicrobial resistance in certain Gram-negative bacteria in the hospital[3].

### 2. Reduced use of antibiotics vs decreased antimicrobial resistance

Reduced consumption of antibiotics could reduce the prevalence of antimicrobial resistance in bacterial pathogens. A classic study in Finland, which had been performed from 1991 to 1996, showed that the reduced consumption of macrolide antibiotics was followed by a steady decrease in the frequency of erythromycin resistance among group A streptococcal isolates from

throat swabs and pus samples from 16.5% in 1992 to 8.6% in 1996[4]. Other study from France also showed that decreased prescription of antibiotics was followed by reduction of penicillin-non-susceptible *S. pneumoniae* colonization[5]. Data suggested that when antibiotic exposure is reduced, antibiotic-susceptible strains recover a survival advantage and subsequently tend to once again become more dominant colonizers.

**IV. Current status of antimicrobial uses in Asia**

- In Turkey, 28% of the subjects were storing antibiotics at home. 19.1% of the subjects were taking antibiotics by themselves without any professional recommendations for sore throat, fever or cough[1].
- In Japan, 60% of the patients who have visited clinics or hospitals were given antibiotics for non-bacterial URI. Third-generation cephalosporins were the most commonly prescribed drug class (46%) followed by macrolides (27%) and quinolones (16%)[6].
- In China, recent data showed that 77.8% of inpatients were given antibiotics among which 55 % were prescribed two or more kinds of antibiotics. In 58% of cases, antibiotics were given therapeutically, but only 39 out of 1,025 cases were investigated microbiologically[7].
- In Korea, 54.7% of the physicians prescribed antibiotics for acute bronchitis, which was presumed viral infection[8].
- In Hong Kong, several surveys showed that antibiotics are being prescribed for ca. 60-80% of cold and flu outpatient visits.
- In Indonesia, 84% of inpatients in two teaching hospitals received antibiotics. Therapeutic uses accounted for 53%, prophylactic uses in 15 % and unclear indication in 32% of cases. Overall, only 21% of antibiotics uses were evaluated appropriate[9].
- In India, according to a recent survey, overall antibiotic prescription rate was 81.8% in primary and secondary healthcare facilities. It was significantly higher in rural hospitals than in urban hospitals. The most common antibiotics used were penicillin, sulfonamides, and fluoroquinolones[10].

**IV. Strategies to control antimicrobial resistance**

The strategies to control and prevent antimicrobial resistance should be based on the factors affecting the emergence and the spread of resistance as described above. The first and the most important strategy is the effective antimicrobial uses which include appropriate use of antibiotics both in the clinical practice and in animal husbandry, strict prohibition of counterfeit drugs, and development of new antibiotics that can be active against resistant pathogens. Since there are many other factors that can also affect the increase in antimicrobial resistance, appropriate use of antimicrobial agents cannot solve the whole problems of antimicrobial resistance. To prevent the spread of antimicrobial resistance, effective and strict infection control in the hospital is very crucial. Because antimicrobial resistance can spread between different countries, international collaboration is also very important. WHO and international organizations such as ANSORP (Asian Network for Surveillance of Resistant Pathogens) and APFID (Asia Pacific Foundation for Infectious Diseases) as well as CDC in respective country should work together on this topic. Vaccination could be another important strategy to control the emergence of antimicrobial resistance. Pneumococcal conjugate vaccine is the best example to reduce the prevalence of antimicrobial resistance in bacterial pathogens. Because there are very few bacterial vaccines that can be used in the clinical practice, new vaccines against major bacterial pathogens should be urgently developed. Finally, appropriate regulations and legal system are very crucial for effective control of resistance. Governmental strategy to contain antimicrobial resistance includes creating a national inter-sectoral task force to raise the awareness of antimicrobial resistance, allocating resources to promote the implementations to contain resistance, and evaluating the impact of the resistance containment strategy.

**V. Campaign programs for appropriate use of antibiotics**

**1. Past and current campaign programs**

A recent analysis showed that there were 22 campaigns done at a national or regional level to promote the appropriate use of antimicrobial agents in the clinical practice between 1990 and 2007 in high-income countries[11]. These campaigns were most frequently done in Europe (16 campaigns), North America (3), Oceania (2), and Israel (1). But, there has been no large-scale public campaign in Asia to date, where antimicrobial resistance is the most serious in the world.

**2. I Care (Initiatives to Control Antimicrobial REsistance)**

I Care is a newly launched international campaign program in Asia which is run by the Asia

Pacific Foundation for Infectious Diseases (APFID). I Care program includes appropriate use of antimicrobial agents, promotion of available vaccination, promotion of more active infection control as well as increasing the public awareness of resistance. The campaign consists of interventions for the public and for healthcare professionals. Interventions for the public include distribution of printed materials, mass media campaign, and providing information by using internet and the social network service. Interventions for healthcare professionals include education of physicians by academic meetings or conferences, treatment guidelines, information sharing through website and social network service. I Care campaign will be done in collaboration with the academic societies and governmental system. Detailed contents of I Care campaign will be presented at ISAAR 2011.

## VI. Conclusion

Antimicrobial resistance is a serious threat to public health worldwide. Comprehensive strategies should be implemented to control and prevent the emergence and the spread of antimicrobial resistance. One of the most important strategy is to promote the appropriate use of antimicrobial agents in the clinical practice. Public campaign is an effort to promote the appropriate use of antimicrobial agents that should be activated in the Asian region where the resistance is the most serious in the world. I Care will be launched to Asian countries from 2011 and is expected to contribute to the future control and prevention of resistance in the region.

## References

1. Ilhan MN, Durukan E, Ilhan SO et al. Self-medication with antibiotics : questionnaire survey among primary care center attendants. Pharmcoepidemiol Drug Safety. 18;1150-57, 2009
2. Goossens H, Ferech M, Stichele RV et al. Outpatient antibiotic use in Europe and association with resistance : a cross-national database study. Lancet. 365;579-87, 2005
3. Hsueh PR, Chen WH, Luh KT. Relationship between antimicrobial use and antimicrobial resistance in Gram-negative bacteria causing nosocomial infections from 1991-2003 at a university hospital in Taiwan. Int J Antimicrob Agents. 26;463-72, 2005
4. Seppala H, Klaukka T, Vuopio-Varkila J, et al. The effect of changes in the consumption of macrolide antibiotics on erythromycin resistance in group A Streptococci in Finland. N Engl J Med. 337;441-46, 1997
5. Guillemot D, Varon E, Bernede C, et al. Reduction of antibiotic use in the community reduces the rate of colonization with penicillin-G nonsusceptible *Streptococcus pneumoniae*. Clin Infect Dis. 41;930-38, 2005
6. Higashi T, fukuhara S. Antibiotic prescription for upper respiratory tract infection in Japan. Intern Med. 48;1369-75, 2009
7. Hu S, Liu X, Peng Y. Assessment of antibiotic prescription in hospitalized patients at a Chinese hospital. J Infect. 46;161-3, 2003

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8. Kim NS, Jang SN, Jang SM. Factors influencing antibiotic prescribing of primary health physicians in acute upper respiratory infections. J Prev Med Public Health 38;1-8, 2005
9. Hadi U, Duerick DO, Lestart ES, et al. Audit of antibiotic prescribing in two governmental teaching hospitals in Indonesia. Clin Microbiol Infect. 14;698-707, 2008
10. Kumar R, Indira K, Rizvi A, et al. Antibiotic prescribing practices in primary and secondary healthcare facilities in Uttar Pradesh, India. J Clin Pharm Therapeut. 33;625-34, 2008
11. Huttner B, Goossens H, Verheij T, et al. Characteristics and outcomes of public campaigns aimed at improving the use of antibiotics in outpatients in high-income countries. Lancet Infect Dis. 10;17-31, 2010