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EDITORIAL

RATIONAL USE OF ANTIBIOTIC

The discovery of antibiotics during 20th century is one of the greatest triumph in the history of medical science. Starting with the introduction of sulphonamides in 1930s, penicillin and streptomycin in 1940s, the broad spectrum bacteriostatic antibiotic in 1950s followed by bactericidal antibiotic in 1960s revolutionized the treatment of bacterial infections.1 The use of these wonder drugs combined with improvements in sanitation and nutrition and the advent of widespread immunization programme has led to a dramatic drop in death from infectious diseases. This achievement is now seriously jeopardized by the emergence of resistant organisms, contributed by the use, misuse and abuse of antibiotic by mankind. The consequences are severe. Infections caused by resistant organism fail to respond to treatment resulting in prolonged illness and greater risk of death. The phenomenon of antibiotic resistance has prompted several WHO meeting with stakeholders in the last decade.

Overuse and inappropriate use of antibiotic accounts for 20-50% of all antibiotics used for humans and animals globally. The Centre for Disease Control and prevention in USA has estimated that some 50-150 million prescriptions in every year are unnecessary.2 It is also observed that countries with highest per capita antibiotic use have the highest resistance rates. Misuse of antibiotic by physician is especially high in intensive care unit of developed countries but misuse of antibiotic by unskilled practitioners and general public is a major problem in developing countries.

The first antibiotic, Penicillin had unbelievable ability to treat the bacterial infections especially those caused by staphylococcus and Streptococcus infections without harming the host. Now a day, more than 95% of those organisms are resistant to Penicillin. By the late 1980s even methicillin resistant staphylococcus aureus had become prevalent in many hospitals and difficult to treat.

Mechanism: Resistance to antimicrobials is a biological phenomenon that can be amplified by a variety of factors including human practices.3 The use of antimicrobials for any infection real or feared, and over any time period forces microbes to either adapt or die in a phenomenon known as "selective pressure". The microbes which adapt and survive carry genes for resistance, which can be passed on. Much evidence supports the view that total consumption of antimicrobials is the critical factor in selecting resistance. Paradoxically, inadequate dosing, poor adherence and substandard antimicrobials play important role as well.

Antibiotic resistance should be defined in terms of clinical outcome rather than by laboratory methods.4 Resistance in bacteria can be intrinsic or acquired. While intrinsic resistance is naturally occurring trait arising from the biology of the organism, while acquired resistance occurs when a previously sensitive bacteria develops resistance afterwards. This frequently happens by mutation or by acquisition of new DNA. Resistance genes produced in the process are replicated and transferred to in-contact individuals via plasmids and transposons. Besides mutation, bacteria might develop a diverse array of biochemical system for ensuring resistance. These include antibiotic modification by enzymatic degradation, reducing antibiotic uptake and quick efflux of it. The

final mechanism by which bacteria protect themselves is the production of an alternative target that is resistant to antibiotic.

Penicillin resistant pneumococci were first reported in Australia and Papua New Guinea in 1960s. Emergence of methicillin resistant staphylococci in 1970 and vancomycin resistance in 2000 is a cause of concern for all clinician. Susceptible enterobacter from burn patient notoriously develops resistance to third generation cephalosporins even with a single course of treatment. Multidrug resistant salmonella typhi emerged in 1987 and has spread throughout the Indian subcontinent, south east Asia and sub-saharan Africa. More alarming is the emergence of multidrug resistant tuberculosis, spreading rapidly and threatening to spiral out of control. The HIV/AIDS pandemic, acting as a catalyst has led the MDR-TB to reach an unprecedented height.

Consequences: The antibiotic resistance to microbes leads to severe consequences.2 Infections caused by resistant microorganisms fails to respond to treatment resulting in prolonged illness, greater risk of death, longer period of hospitalizations and infections which increases the number of infected people in the community. When an infection becomes resistant to first line antibiotic, treatment has to be switched to second or third line antibiotic which are always much more expensive and toxic as well. Current trends suggest that infectious disease will have no effective therapies in the next decade.

Contributory factors: Achievement of judicious prescription of an antibiotic primarily requires an understanding of the factors that promotes overuse.1 Both the provider and patients are equally responsible for different factors: (a) Lack of education- The provider approach suboptimally to diagnose and treat and patient do not understand the treatment difference between bacterial and viral infections. (b) Experience- It poses a difficulty in changing prescribing habits and public has false reliance on antibiotic (c) Expectations- Doctor believes that patients expect antibiotic and patient relies on antibiotics for any infections (d) Economics- Incentives are related with antibiotic prescription and patients need to get cured and return to work quickly. (e) Others-Besides random prescription by quack in developing countries poor compliance, treatment interruption and self medication by the patients also add to this problem. Antibiotic exposed to harsh adverse condition during shipment to tropics and expired drugs receiving new level also promotes development of resistance.

Antibiotic is misused in different ways such as wrong empiric antibiotic choice, underdosing of antibiotic, using an antibiotic that does not penetrate the area of infection, using second line antibiotic when first line is effective and using broad spectrum antibiotic when narrow spectrum is sufficient.3 Similarly, antibiotic overuse is done by prescribing antibiotic for nonbacterial infections, administering prophylactic antibiotic, continuing antibiotic past the resolution of infections, and administering antibiotic based on investigation ignoring the clinical evidence. Possible reasons for antibiotic use by doctors are lack of confidence, poor knowledge of antibiotic pharmacokinetics, poor understanding of sensitivity pattern and satisfying the patients expectation.

In the past few decades, the development of resistant organism has been greatly accelerated by several concurrent trends.1 Such trends include- (a) urbanization with its associatied overcrowding and poor sanitation (b) pollution, environmental degradation and changing weather pattern (c) growing population of elderly people needing hospital care (e) enlarged population of immuno-compromised patients (f) resurgences of old infections- malaria & tuberculosis and (g) growth of global trade and travel.

Veterinary prescription of antimicrobials also contributes to the problem of resistance.4 In North America and Europe 50% of production of all antibiotic is used in food producing animals and poultry. It is used to promote growth by small amount of food, prevent and treat infectious disease. Resistant organism in animals contaminates the meat and animal products and consumed by humans. Besides this, antibiotic given to animals remain in animal meats and eventually consumed by humans which exert selective pressure on human bacteria to become resistant.

When there is a cry for new antibacterial drug, the hope for a novel agent is practically bleak.5 After 2000, nearly hundred drugs has been approved by Food and Drug Administration, USA but very few of them are antibiotic eg, linezolid, daptomycin, gemifloxacin.

Intervention: In September 2001, WHO launched the first global strategy for combating the serious problems caused by the emergence and spread of antimicrobial resistance known as WHO Global Strategy for Containment of Antimicrobial Resistance.1 It helps countries to establish laboratory based networks for the surveillance of resistance. Prior to this WHO has produced model list of essential drugs in order to help government select the most effective and appropriate drugs in line with the priority needs. A concerted international effort is required to reduce antimicrobial resistance. Intervention strategies must be supported by national and local policies. National goals should be developed to reduce unnecessary use and progress towards this goal should be monitored.

Intervention strategies should be targeted to both the doctors and patients. Doctors can be enlighted by developing clinical practice guideline, distribution of supportive materials, direct mailing of information and providing feedback to their enquiry. Patients and public can be educated both at home and hospital using different print and electronic media by the health care personnel. Besides updating of medical and veterinary practice guideline, better diagnostic tests, prevention of sale from over the counter and development of novel antibiotic are some of the important steps required now.

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