Virtues, shortcomings and future development of antibiotic therapy

Introduction

In the pre-antibiotic era, a small cut or scratch was abundant to kill a human being. Delivering a child and surgeries such as organ transplant also took life of many as it often caused bacteremia and septicemia. In those times, sole treatment for communicable diseases was fresh air and rest and people had to count on their immune system to get cured. According to CDC. National Centre for Health Statistics for Life expectancy, the average life expectancy at birth was 47 years (46 and 48 years for men and women respectively) even in the industrialized world. Infectious diseases such as smallpox, cholera, diphtheria, pneumonia, typhoid fever, plague, tuberculosis, typhus, syphilis, etc. were rampant (as cited in Treasure called Antibiotics, 2016).

Thanks to Sir Alexander Fleming, a Scottish bacteriologist working at St. Mary’s Hospital who left his office cluttered before going on a vacation. It caused growth of mold on Petri dishes which appeared to be destroying bacteria surrounding it and this mold lead to the discovery of penicillin. Later, Gerhard Domagk and Selman Waksman discovered other classes of antibiotics which totally revolutionized the field of medicine. The discovery of antibiotics significantly decreased death by communicable diseases and enhanced life expectancy all around the globe. Today, antibiotics are blessing for those who are born with or acquired immune deficiency because of diseases, for example, AIDS or medical procedures such as chemotherapy or surgeries. Furthermore, nowadays there are only scarce probabilities for any transmissible disease or septic wound to become fetal. At the global level, there has been a one-third drop in TB deaths, falling from 1. 8 million in 1990 to 1. 2 million in 2016 (Ritchie & Roser, 2018). Unfortunately,

practitioners and people have over exploited antibiotics which have not only made these valuable medicines less and even ineffective in several cases but also lead to creation of new powerful strains of bacteria which are resilient to most of the antibiotics. This paper confers about the process of action, benefits, and harms of antibiotic use in the modern healthcare system and other areas followed by some solutions to lessen abuse of antibiotics and discussion about the future of antibiotics.

Classes and Mechanism of action

Due to specific host defenses, our body can protect us from a range of illnesses. These defenses include actual physical barriers such as skin and respiratory mucosa or physiological defenses such as HCl acid in our stomach and antibodies present in our bodily fluid (Lilley, Harrington, Snyder, & Swart, 2011). Often, our body’s host defenses are insufficient for protecting us from harmful microorganisms invading our body and for dealing with this problem, antibiotics are incorporated. The type of antibiotic to be used mainly depends on the morphology of bacteria. The prominent procedure for testing this is Gram-Stain procedure. Species that stain purple with the Gram-stain dyes are classified as gram-positive and they have a thicker cell wall as well as thicker outer cell capsule. Those which stain red are classified as gram-negative and have a complex cell wall with smaller outer capsule (Lilley, Harrington, Snyder, & Swart, 2011). This makes treating gram-negative infections harder because of the complexity of their cell walls. Most of the antibiotics generally interfere with protein synthesis, replication of RNA and DNA and encroach crucial reactions that are necessary for metabolism. A crucial factor that disrupts mechanism of

antibiotics if genetic abnormalities and enzyme deficiencies such as glucose-6-phosphate dehydrogenase (6GPD) deficiency. Hence, it is important to take these factors into consideration while choosing appropriate medicine.

There are several distinct types of antibiotics available today such as penicillin, sulfonamides, macrolides, aminoglycosides, cephalosporins, and tetracyclines. Sulfonamides are synthetically derived from sulfanilamide which is the first sulfonamide discovered (Lilley, Harrington, Snyder, & Swart, 2011). These drugs are bacteriostatic antibiotics and intervene with B complex and folic acid synthesis in the cell hence, hindering the metabolic activity which earned them the name antimetabolites. Commonly, sulfadiazine, sulfamethoxazole, sulfisoxazole are prescribed as a single drug and trimethoprim and sulfonamide are used in synergy.

β – Lactam antibiotics comprise four chief drugs that are penicillin, cephalosporin, carbapenems and monobactams and all of these have a β – Lactam ring in their structure. Some bacteria can show resistance to these drugs as they have an enzyme β – Lactamase that dissolves β – Lactam ring and causes the drug to lose efficacy. Therefore, β – Lactam antibiotics are used in collaboration with β – lactamase inhibitors to counteract dissolving of the ring and to boost their effectiveness. Broad Spectrum Antibiotics were the first antibiotics to be discovered and were used in world war II (Lilley, Harrington, Snyder, & Swart, 2011). They have bactericidal properties which enable them to kill a wide range of bacteria. One of those is Penicillin which is obtained from mould fungus. Its molecules generally penetrate the cell wall of bacteria and if they are not small enough to pierce they attach themselves with other sites of the cells called penicillin-binding sites and

afterward, they disrupt the normal cell wall synthesis and cause death of the cell by rupture. There is another class of antibiotics that physically and pharmacologically resembles to penicillin called Cephalosporin which is a synthetically transformed antibiotic. It has similar bactericidal properties as penicillin and it binds with same penicillin binding sites. Another class of antibiotics is Macrolides which can either exhibit bactericidal or bacteriostatic properties based on its dilution and dosage. They are more effective in eradicating some of the species of bacteria and can easily penetrate the cell walls. Moving further, there is a sort of antibiotics called aminoglycosides which is particularly used for virulent infections, but it has some adversative effects such as ototoxicity and nephrotoxicity if not monitored properly (Lilley, Harrington, Snyder, & Swart, 2011). Furthermore, commonly known as quinolones, fluoroquinolones are potent, bactericidal, broad-spectrum antibiotics that destroy bacteria in a slightly similar manner as sulfonamides that is, by altering their DNA. These are mostly utilized when treating sexually transmitted, respiratory, bone, skin and gastrointestinal illnesses.

Overuse of antibiotics

The discoverer of world’s first antibiotic himself warned the world about future abuse of this medicine. As Fleming supposed, “ The thoughtless person playing with penicillin treatment is morally responsible for the death of the man who succumbs to infection with the penicillin-resistant organism” regretfully, it has become the reality of today’s world. In an analysis of the IMS Health Midas database, which estimates antibiotic consumption based on the volume of antibiotics sold in retail and hospital pharmacies, it is

indicated that in 2010, 22. 0 standard units (a unit equaling one dose, i. e., one pill, capsule, or ampoule) of antibiotics were prescribed per person in the U. S (as cited in Ventola & Lee, 2015). In an investigation of antibiotic prescribing practices during ambulatory care visits in the United States, it was discovered that an estimated 154 million prescriptions for antibiotics were written in ambulatory care settings per annum during 2010-2011 and out of that 30% of outpatient, oral antibiotic prescriptions were not necessary (Fleming, AL, & Sharpiro). The condition worsens in winter months as people run for getting antibiotics for common flu and cold which are not even bacterial but viral diseases. A study has shown there is a significant difference between consumption of antibiotics in winter compared to other months. Antibiotic prescriptions in the U. S were 24. 5% higher in winter months than in the summer, with the largest difference (28. 8%) in 2008 and the smallest (20. 4%) in 2010 (Suda, Hicks, Roberts, Hunkler & Taylor, 2014). The chief reason accelerating enormous consumption of antibiotic usage is incorrect diagnoses and abuse of drugs for treating minor health issues such as common cold. Studies have depicted that treatment indication, choice of agent, or duration of antibiotic therapy is incorrect in 30% to 50% of cases (Luyt, Bréchot, Trouillet, Chastr, 2015 as cited in Ventola & Lee, 2015). Also, many people are unaware of the harms of antibiotic overuse which causes them to seek antibiotic as an answer to all their health issues. Furthermore, Martin Blazer has aptly said in his book Missing Microbes that habits are ingrained, people are terrified of germs (2014). There is a social stigma that ‘ germs are bad’ which drives people towards excessive use of oral and topical antibiotics and sanitizers. This suppresses our natural immunity towards environmental antigens. That might be the answer why numerous kids suffer

asthma, obesity allergies, and autoimmune diseases. These ailments were not common in the children in the past, maybe because then the times were simple, and children could eat and roll in the mud unlike now where mothers keep piles of disinfectant wipes, hand sanitizers and disinfecting tablets at home to keep their child germ free. Another factor that worsens this issue is cheap price and easy availability of antibiotics. Nowadays most of the antibiotics are available over the counter or online in many nations. This lack of regulation has made antibiotics easily accessible, plentiful, and cheap, which promotes overuse (Michael, 2014 as cited in Ventola & Lee, 2015).

Not only health care sector, but the farmers who rear livestock for poultry, meat and milk are also responsible for antibiotic abuse. In the past, the arrival of antibiotics improved life expectancy and declined mortality rate which lead to sudden population explosion. This population outburst further increased demand for meat and poultry. To meet these demands farmers began using antibiotics in small amounts to hasten the growth of the animals. Little did they knew, that this might lead to an expansion of antibacterial resistance. Today a massive amount of antibiotic medicine is being used by farmers as a growth supplement. An estimated 80% of antibiotics sold in the U. S. are used in animals, primarily to promote growth and to prevent infection (Spellberg & Gilbert DN 2013; Gross M, 2013 as cited in Ventola & Lee, 2015). Chronic usage of antibacterial drugs in farming practices enables strains of bacteria to develop resistance and these resistant bacteria are passed from animals to humans. It also disrupts natural microbiome and kills useful species of bacteria living in environment as 90% of the antibiotics given to livestock are excreted in urine and stool,

then widely dispersed through fertilizer, groundwater, and surface runoff (Centers for Disease Control and Prevention, Office of Infectious Disease Antibiotic resistance threats in the United States, 2013 as cited in Ventola & Lee, 2015). It further interrupts the proportion of bacteria by increasing resistant ones and decreasing vulnerable one and it enables the resistant bacteria to grow their population and share their DNA with others.

Antibiotic Resistance and Superbugs

Due to overuse of antibiotics world is experiencing serious antibiotic resistance catastrophe. Antibiotic resistance is a term used for bacteria's capability adapt to drugs through frequent exposure and hence become invincible. These powerful strains of bacteria also called superbugs then replicate and share their DNA and coping mechanisms with other bacteria. This phenomenon is akin to Darwin's theory of survival of the fittest. Antibiotic-resistant infections are already widespread in the U. S. and across the globe (Golkar, 2014 as cited in Ventola & Lee, 2015). Due to antibiotic resistance, we have created a similar situation as a pre-antibiotic era where almost all infectious diseases were fetal. The condition is particularly worse in rural nations as medical and hygiene facilities are insufficient in those areas. Antibiotic-resistant infections are hard to treat as they require high doses of medication and most of the antibiotics we have at present time are not capable enough to treat them. Sadly, antibiotic-resistant infections are now commonly seen and are major health concern. A recent study done by the Centers for Disease Control and Prevention (CDC) publication estimated that about 2 million people develop infections with antibiotic-resistant pathogens each year; of those who develop infections, an estimated 23, 000

people die each year as a direct result of these infections (Antibiotic / Antimicrobial Resistance (AR / AMR), 2013).

As Ramanan Laxminarayan said in one of his TED talks, we are playing a game of coevolution with the bacteria, like Cheetahs and Gazelles, the former has evolved to run faster to hunt and the latter have learned the same skill to prevent itself from becoming a prey. In this game, we are not the cheetahs but the gazelles. In a matter of seconds bacteria can have grandkids but we, on the other hand, we have drug discovery processes, screening molecules, we have clinical trials, FDA regulatory process and once we go through all of that, then we try to stay one step ahead of the bacteria (TEDMED, 2014). This statement suggests us how critical the situation is and how less time we have to address the problem.

Solutions

To prevent health hazards and further damage to microbiome the only step we can take is to reduce the consumption of antibiotics. This would require careful examination of ailment before going for antibiotic treatment. Health care providers and patients should together work in a therapeutic relationship to decide whether it is obligatory to use antibiotics or not. An ideal example of it is efforts done by French health authorities in 2002 to reduce antibiotic consumption. They launched the national plan to preserve antibiotic efficacy (Blaser, 2014). Their primary focus was on a prescription of antibiotics to children for viral infection in the winter season. This program enabled them to reduce the rate of prescription by a quarter by changing attitudes of both patients and doctors regarding antibiotic consumption.

Moving further, it is the accountability of health care authorities to aware the public regarding possible health jeopardies which overuse of antibiotics cause. One such step was taken in the UK. They formed a Treat Antibiotics Responsibly, Guidance, Education, Tools (TARGET) toolkit for practitioners and patients which consists of posters and leaflets to share with patient and interactive workshops. It effectively ensures optimal antibiotic prescribing and promotes awareness.

Another important step is using antibiotics in food animals only when it is mandatory for instance, antibiotic usage is justified when an animal is sick. A great example of it is FDA and U. S. Department of Agriculture (USDA) which are doing a immense effort to ensure better and reasonable use of antibiotic in veterinary medicine and agriculture. (Antibiotic / Antimicrobial Resistance (AR / AMR), 2013).

Lastly, rather than being reliant on antibacterial sanitizers and medication people should try to use more traditional ways. Sometimes simple handwashing with soap is sufficient for us and it also protects healthy and useful bacteria living on our skin (Blaser, 2014).

Future of antibiotic medicine

As most of the antibiotics we have at present time seem ineffective against powerful superbugs, we might need new antibiotics with a totally unique mechanism of action. But unfortunately, it is not as easier as it sounds.

Further discovery of new antibiotics is a tough task to do as it is a time consuming and complex process, also, more than 140 antibiotics have

already been discovered for human use which makes the task even more difficult (Spellberg & Brad, 2014). Furthermore, these scientific discoveries might be expensive, and we have an additional economic barrier that is, companies are more attracted to finance those medications which are used for long-term health issues such as asthma and diabetes rather than short-term therapies like antibiotics. Another obstacle is clinical trial regulated by FDA which now has even more unachievable design than the past. This is mainly due to past mistakes in pharmaceutical industries for instance, only if clinical trials of thalidomide were seriously conducted it could save the life of thousands of people. Careful examination of possible effects of a medication on a patient is must and with the current regulations and standards, these tests might take years. All these reasons have marked a decrease in the number of companies and the scientific experts, working in this area (Spellberg & Brad, 2014).

To overcome these obstacles, authorities should take steps to allocate funds to antibiotic research. One possible solution is to raise the prices of antibiotics and use the generated money for antibiotic research. It will not only decrease the usage of antibiotic medicine but will also draw the attention of companies. As well, regulatory processes should be made less time consuming and more feasible for smooth antibiotic development.

Conclusion

The advent of antibiotics not only modernized health care system but also enhanced longevity. Earlier, both patients and doctors were helpless against infectious diseases and antibiotics proved to be a wonder drug for them.

Since its discovery, it has saved the lives of a plethora of people. Sadly, people have abused this marvelous medication to large extent and have created health hazards for themselves and upcoming generations. With excessive use, people have diminished the effectiveness of antibiotics against infection and have damaged the natural microbiome as well. The only plausible solution for this global issue is stewardship of antibiotics and limiting the consumption until new forms of potent antibiotics are discovered. If concrete steps are not taken, those days are not far when humanity will slip back into days of the pre-antibiotic era.

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