ejpmr, 2021,8(12), 85-92

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

A REVIEW ON PRESCRIPTION PATTERN OF ANTIBIOTIC AND ANTIBIOTIC RESISTANCE

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Article Received on 29/09/2021 **Article Revised on 19/10/2021** **Article Accepted on 09/11/2021**

1. ABSTRACT

The overall aim of the review was to present and describe the prescription pattern, adverse effects of antibiotics and antibiotic resistance. This review discusses about the high risk drugs such as anthracyclines, Linezolid and fluoroquinolones are used to increase the likelihood of drug related morbidity and mortality. Patient factors in pregnancy that can increase the risk of drug harms include fetus death, growth retardation and congenital abnormalities. The prescribing pattern of antibiotics is used to reduce the irrational prescribing of medicines. Irrational prescribing of medicines results in serious morbidity, mortality, economic burden and it leads to reduce the quality of patient care. So, WHO has introduced indicators in three main drug use areas like prescribing, patient care, facility specific factors. The study discusses the disaster of antibiotic resistance as an ongoing international health risk with the side effects of antibiotic and highlights efforts to mitigate this complex problem. Now-a-days, antibiotic resistance has to become a rapid and major clinical problem to the worldwide population. The number of infections caused by antibiotic-resistant bacteria is increasing, and the supply of new antibiotics is very limited. Generally speaking, Community pharmacists can play a potential role in providing consultation to patients. SHEA(The society for health care epidemiology of America) , IDSA(Infectious diseases society of America) and PIDS(Pediatric infectious diseases society) recommend that the centers for Medicare and Medicaid services (CMS) require participating healthcare institutions to develop and implement antimicrobial management plans. The development of new antimicrobial stewardship programs for primary care and hospital by the department of health‘s advisory committee on antimicrobial resistance and healthcare association infection. These programs appear useful in reducing rates of antibiotics resistance. Antibiotic management has been revised the title," Smart-Start-Focus" to encourage clinicians. Steps can be taken at all level of society like Individuals, policy makers, health professionals, healthcare industry and agriculture sector.

KEYWORDS: Prescription pattern, adverse effects, antibiotic resistance crisis, antimicrobial stewardship programs, pharmacist role.

2. INTRODUCTION

Antibiotics are drugs used to prevent and treat bacterial infections. When bacteria change due to the use of these drugs, antibiotic resistance develops.[1] In rare cases, potentially long lasting adverse effects reported with antibiotics to evaluate and compare the efficacy and safety of patient. Harmful consequences of antibiotics are usually indicted by pathological changes detected as morbidity, mortality, weight changes, level of enzymes, loss of function, etc. it can also be indicated by symptoms reported by the patient. Side effects can cause reversible and irreversible changes including an increase and decrease in an individual's susceptibility to produces such as interaction with other chemicals, foods, or drugs. Improper antibiotic prescribing is a public health problem for the entire population, leading to antibiotic resistance. Understanding antibiotic prescribing patterns is crucial in addressing inappropriate prescribing.[2] The most commonly prescribed antibiotics are Cephalosporins. Antibiotic resistance is ancient, and resistance is a dynamic and ongoing problem.[3] According to reports, when a drug losses its ability to effectively inhibit the growth of bacteria, it will resistance. In the presence of therapeutic level of antibiotics, bacteria become "resistant" and continue to multiply.[4] Antibiotic stewardship has been defined in a consensus statement from the IDSA, SHEA, PIDS as "coordinated interventions designed to improve and measure the appropriate use of [antibiotics] agents by promoting the selection of the optimal [antibiotic]drug regimen including dosing, duration of therapy and route of administration.[5] In an era, where AR() is a ticking time bomb, stringent measures in prescribing and dispensing antibiotics should be followed, with a view of making pharmacist counseling on every antibiotic prescription compulsory.[6]

3. PRESCRIPTION PATTERN OF ANTIBIOTICS

The study of prescribing patterns seeks to monitor, evaluate and suggest modifications in practitioners prescribing habits to make the medical care more rational.[2] The antibiotic treatment regimens given in the most of patients were without done culture sensitivity test before prescription which leads to irrational prescribing. Rational prescribing of antibiotics avoids polypharmacy and prevents antibiotic resistance. Cephalosporins are generally widely prescribed due to their high potent action, available in various formulations in the market, their extended indication and the activity against the gram negative to gram positive bacteria means broad spectrum activity from first generation to third generation of Cephalosporins.[7] >58.9% of antibiotics prescribed for patients admitted to surgical ward. Ceftriaxone was most commonly prescribed by physicians (24.5%). Ampicillin was most frequently prescribed antibiotics on gynecology, obstetrics as prophylaxis. 49% of patients received single antibiotic, 39% of patients received combination antibiotics. Drug utilization was tested by WHO core drug use indicators such as prescribing and health facility indicators. Total no. of drugs prescribed, average no. of drugs/prescription, percentage of antibiotics prescribed were mentioned.[2]

Table 1: List of Antibiotics Prescribed.[8]

LIST OF ANTIBIOTICS	PERCENTAGE OF ANTIBIOTICS PRESCRIBED
Ceftriaxone	69 (19.2)
Amoxicillin-Clavulanic acid	61 (16.9)
Pencillin-Tazobactam	41 (11.4)
Metronidazole	25 (6.9)
Cefixime	16 (4.4)
Ciprofloxacin	16 (4.4)
Azithromycin	14 (3.8)
Levofloxacin	14 (3.8)
Norfloxacin	14 (3.8)
Clindamycin	11 (3.1)
Amikacin	10 (2.7)
Vancomycin	9 (2.5)
Moxifloxacin	8 (2.2)
Ofloxacin	7 (1.9)
Rifamin	5 (1.4)
Isoniazid	4 (1.1)
Rifampicin	4 (1.1)
Pyrazinamide	4 (1.1)
Ethambutol	4 (1.1)
Gentamicin	3 (0.8)
Imipenam	2 (0.5)
Chloramphenicol	1 (0.3)
Cefaperazone and sulbactum	1 (0.3)

4. ADVERSE EFFECT OF ANTIBIOTICS

4.1. ANTHRACYCLINES

Cases of pregnant women with acute leukemia (AL), aggressive Non-Hodgkin's Lymphoma (NHL), or Hodgkin's Lymphoma (HL), which is treated by anthracyclines chemotherapy with doxorubin or daunorubicin, idarubicin. The adverse effect of these drugs are fetal toxicities were death, growth retardation and congenital abnormalities. The drug Idarubicin associated with fetal cardiomyopathy.[9]

4.2. CARBAPENEMS (CBP)

A retrospective study of CBP was performed over 10 month period. Data collected from bacteriological analysis results and infectious disease physician. Infections are microbiologically documented, and ESBL (EXTENDED SPECTURM BETA LACTAMASE) bacteria accounted for 69% and 5 of ESBL isolates were acquired from the community. The mostly used carbapenems and imipenem (57%), ertopenem (38%), meropenem (5%). The major adverse effects of carbapenems are urinary tract infection (61%), pneumonia (25%) infections were nosocomial (59%).[10]

4.3. FLUOROQUINOLONES AND QUINOLONES

Prolonged adverse events have been reported with systemic and inhaled quinolones and fluroquinolones. 63.7% of adverse reactions were reported as serious, 28.7%resulted in hospitalization, 4.5% with persistent /severe disability. The most common side effects these days affecting the peripheral and central nervous system, tendon, muscle and joints are reported by the Pharmacovigilance center (PVC).[11]

4.4. LINEZOLID

In 28daystreatment plan in 280 cases, hematologic adverse reaction were reported mostly blood cell counts decreases.

14 people: suppression of atleast one myeloid cell line
7 people: required transfusion
2 people: diarrhea, skin reaction, vomiting, asthenia were observed
Linezolid drug are used in neurosurgery patient, major ADR are asthenia (100%), anorexia (37.5%), peripheral neuropathy (37.5%), anemia (25%), hyperviscosity syndrome (62.5%).[12]

4.5. LINEZOLID AND VORICONAZOLE

Voriconazole (VCZ) - serum baseline concentrations before treatment with Linezolid (LIN) and analysed by liquid chromatography. Adding LIN and VCZ treatment increases VCZ clearance between 250%-100% and serum antifungal concentrations decreases clinically. Use of this combination is contraindicated.[13]

5. ANTIBIOTIC RESISTANCE CRISIS

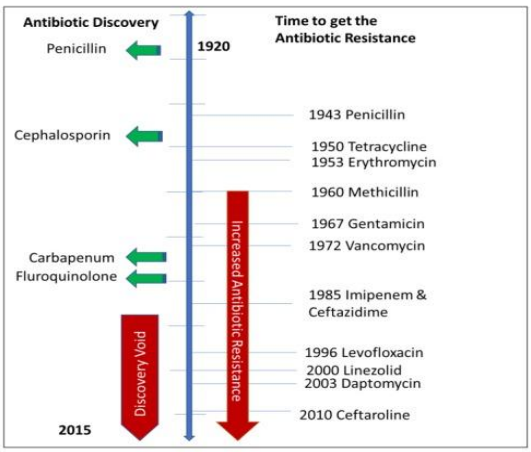
Antibiotic resistant is ancient and the "resistome" is a dynamic and mounting problem. Antibiotic resistance develops wherever antibiotics are used in agriculture as much as healthcare.[14] Resistance leading to treatment failure and/or death affects a vast array of medical condition and procedure including cancer, pneumonia, infant blood stream infection and organ transplantation. The antibiotic resistance crisis is exacerbated by gram-negative pathogens[15]; Strains resistant to several antibiotics have emerged among the major gram-positive and gram-negative species, including Staphylococcus aureus, Enterococcus spp, Enterobacteriaceae and Neisseria gonorrhea.[18]

6. DISCOVERY OF ANTIBIOTIC RESISTANCE

The discovery of antibiotics is a watershed in human history, revolutionizing medicine and saving countless lives. Unfortunately, these "magic bullets" are accompanied by these emerging resistant pathogen strains.[17]

Antibiotic resistance to multiple antimicrobial agents was first discovered in the gut micro biota Salmonella, Shigella and E. coli in the late 1950s and early 1960s. These resistance strains cause huge clinical, economic losses and loss of life mainly developing world. In 1970s when it was observed the neisseria gonorrhea and haemophilus influenza are resistant to ampicillin, while in the case of haemophilus it was further reported to resist tetracycline and Chloramphenicol as well.[18] [19] According to CDC (Centers for Disease Control and Prevention) declared in 2013 that the human race is now in the "Post antibiotic era". In 2014, the WHO warned that the antibiotic resistance crisis is becoming dire.[20]

Graphical representation of onset of antibiotic resistance versus time to get antibiotic resistance
History of antibiotic discovery (Green Arrow) and time of first reported year of antibiotic resistance (Right side). The Red arrow (Lower Direction) indicates the discovery void and increases the antibiotic resistance. The blue line indicates the time flow.[23]



Illegal use of antibiotic can make microorganisms resistant to drugs. Since the introduction of sulfa drugs in 1937, specific resistance and mechanisms have been developed and used for therapeutic purposes. However, resistance of sulfa drugs was reported in the 1930s, showing the same resistance mechanism, which is still effective 80 years late, within 6 years of the production of aminoglycosides[22] yellow. Aminoglycoside resistant staphylococcus aureus strains have been developed.[24] The first semi-synthetic penicillinase-resistant penicillin introduced in 1961, targeting methicillin-producing staphylococcal strains. However, methicillin resistance was reported shortly after the start.[25] 44 years after Vancomycin was introduced to the market, a recent clinical isolate of Vancomycin-resistant Staphylococcus aureus (VRSA) was discovered in 2002.[26] [27]

7. SCOPE OF PROBLEM

- The overuse and misuse of antibiotics clearly drives the crisis and evolution of antibiotic resistance.[31]
- In many countries where standard treatment guidelines are not available, antibiotics are often

over-prescribed by health-care workers and veterinarians and over-used by the general public.[1]

- Antibiotic resistance can affect all age peoples in any country.[1]
- Resistant bacteria spread from humans to animals and vice versa.[15] In some developed countries, animals take antibiotics in food, water or parenteral, which may be the cause of microbial resistance to these specific antibiotics.[28] For example, the use of antibiotics as growth promoters in livestock feed can increase antibiotic resistance.[29]
- The use of one antibiotic can lead to resistance to multiple drugs, because bacteria tend to accumulate resistance.[15]
- In recent decades, multidrug resistant bacteria have increased at an alarming rate and caused serious problems.[30]
- Causes of "global resistome" are overpopulation, enhanced global migration, increased risk use of antibiotics in clinics and animal production, selection pressure, poor sanitation, wild life spread and poor sewage disposal system.[16] [39]
- When antibiotics for humans or animals can be purchased without a prescription, the emergence and spread of drug resistance worsens.[1]
- The CDC assessed antibiotic-resistant bacterial injection according to seven factors: clinical impact, economical impact, transmissibility, availability of effective antibiotics, and barrier to prevention incidence, 10 years project of incidence.[31]

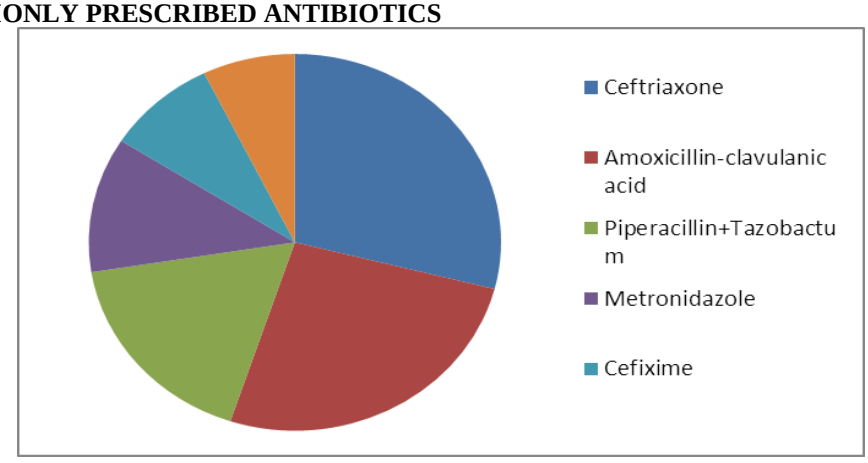
8. DEVELOPMENT OF RESISTANCE TO ANTIBIOTICS

The emergence of drug-resistant infections caused by these bacteria has leads to morbidity and mortality, and there is an urgent need to find a solution to the resistance of the bacteria.[30] Studies have shown that treatment indication, choice of agent or duration of antibiotic therapy is incorrect in 30%-505% of cases. In addition 30%-60% of antibiotics prescribed in Intensive Care Units (ICUs) have been found to be unnecessary, inappropriate or suboptimal.[21] [28] Another valuable input to the issue has been the recent publication of the book filled "The evolving threat of antimicrobial resistance –options for action". In the UK, people voted for government-sponsored prize of £ 10 million / longitude prize challenges to create novel solution in combating antibiotic resistance.[33] Studies confirmed that sulfamethoxazole and trimethoprim (TMP-SMZ), ampicillin and tetracycline that were commonly used in yester years, but now have no longer role in treating non-cholera, diarrhea diseases in Thailand.[34] At the same time, another study conducted in Bangladesh should the effectiveness of the same drug in treating the effectively.[35] In fact resistance was documented even before the beginning of the usage of antibiotic in fighting the infection.[36] Antibiotic-resistant infections and considerable costs to the nation's already overburdened health care system when first-line and second-line antibiotics treatment options are limited or unavailable, Health care professionals may be forced to use antibiotics that are more toxic to the patient and frequently more expensive.[31] [38]

DISCUSSION

The antibiotic treatment plan of most patients did not undergo a culture susceptibility test before prescription, resulting in unreasonable prescription. The reasonable prescription of antibiotics avoids multiple medications and prevent antibiotics avoids multiple medications and prevents antibiotic resistance. Inappropriate use of antimicrobials may cause viral infection had the study been conducted during the time had been reported previously. The percentage (>65%) of prescription contain broad spectrum antimicrobials (amoxicillin, Clindamycin, piperacillin-tozabactum).[42] Total no. of drugs prescribed, average no. of drugs/prescription, percentage of antibiotics prescribed were mentioned.

LIST OF COMMONLY PRESCRIBED ANTIBIOTICS



The main method of detecting the potential ADRs over the last half century in is the voluntary reporting system operated by the yellow card scheme, medicines and healthcare products regulatory authority (MHRA) and

human drugs commission (CHM) in the United Kingdom (UK). Pharmacist -directed Antibiotic Management programs (SPSA) have grown dramatically over the past decade. Following evidence that these programs improve patient care, the infectious diseases society of America and the American society of health care epidemiology have published ASP development guidelines the define the clinical pharmacist trained in infectious diseases as a essential member.[40] [41]

ANTIMICROBIAL STEWARDSHIP PROGRAMS

Controlling AR requires a multifaceted approach. An antimicrobial stewardship program (ASP)is an approach that can be used to improve antibiotic resistance.[43] Antibiotic stewardship has been identified in a consensus statement from the IDSA, SHEA, and PIDS as "coordinated interventions designed to improve and measure the appropriate use of [antibiotics] agents. Drug regimen, including dosage, duration of treatment and route of administration".[5] The main goal of an ASP is to improve efficacy, minimize adverse effects and unintended consequences of antibiotic use and limit the spread of antibiotic resistance. ASPs also aim to improve the cost effectiveness of antimicrobials treatments.[43] This has been revised, and has been superseded by the ARHAI antimicrobial management guidelines since November 2011, titled 'start smart-The focus'which aims to encourage clinicians.[44] [45]

START SMART

Get culture first: knowing the susceptibility of infectious organisms can reduce broad – spectrum therapy, and when culture indicates that infection is unlikely to occur, switch treatment to effective antibiotics.

- PRESCRIBE: A single dose is used for surgical prophylaxis where antibiotics have been shown to be effective. The key to this initiative I to administer a single dose about 60 minutes before the surgical incision to reach the maximum blood levels at the beginning of the operation when the operating time exceeds the half-life of antibiotics, repeated doses of antibiotic prophylaxis are required patients undergoing surgery on dirty or infected wounds should be treated with antibiotics (expert prophylaxis)(surgical prophylaxis).

THE FOCUS

The five antibiotic stewardship decision options are stop (stop antibiotics if there is no signs of the infection, switch (switch from intravenous to oral antibiotics), change (change antibiotics-ideally to a narrower spectrum, if more is needed), continued (continue and review again at 72 h) and OPAT.

- Review the clinical diagnosis and the need for continuing antibiotics by 48h before. Make an aggressive antimicrobials management decision to stop, switch, change, continue or move to outpatient parenteral antibiotic therapy (OPAT). Antibiotics are generally started before a patient's full clinical picture is known. By 48h, when additional microbiology, radiographic and clinical information for clinicians to revaluate why the therapy was initiated in the first place and to gather evidence on whether there should be made and documented in the notes for all patients on antibiotics (adult and children).[44]

GLOBAL ACTION PLANS AND AWARNESS

A global action plan to the tackle the growing problem of resistance to antibiotics and other antimicrobial medicines was endorsed at the sixty-eight world health assembly in May 2015.Step can be taken at all level of society to reduce the impact and limit the spread of resistance.

INDIVIDUALS

To prevent and control the spread of antibiotic resistance, individuals:

- Only use antibiotics when prescribed by a certified health professional.
- Never demand antibiotics if your health worker says you don't need them.
- Never share (or) use leftover antibiotics.
- Prevent infection by regularly washing hands, preparing food hygienically, avoiding close contact with sick people, practicing safer sex, and keeping vaccinations up to date.

POILCY MAKER

To prevent and control the spread of antibiotics resistance, policy makers can:

- Improve surveillance of antibiotics -resistant infection.
- Strengthen policies, programs and implementation of infection prevention and control-measures.
- Regulate and promote the appropriate use and disposal of quality medicines.
- Make information available on the impact of antibiotic resistance.

HEALTH PROFESSIONAL

To prevent and control the spread of antibiotic resistance, health professional can:

- Report antibiotic resistance infections to surveillance teams.
- Talk to your patient about how to take antibiotics correctly, antibiotic resistance and the dangers of misuse.

HEALTHCARE INDUSTRY

- To prevent and control the spread of antibiotic resistance, the healthcare industry can:
- Invest in research and development of new antibiotics, vaccines, diagnostics and tools.

ARICULTURE SECTOR

To prevent and control the antibiotic resistance, the agriculture sector

- Only give antibiotics to animals under veterinary supervision.
- Not use antibiotics to animal under veterinary supervision.
- Vaccinate animals to reduce the need for antibiotics and use alternatives to antibiotics when available.[46]

ANTIBIOTIC AWARESS WEEK

The World Health Organization launched the first global antibiotic awareness week from November 16-22, 2015. The purpose of this week is to raise global awareness of antibiotic resistance, and hope to promote the correct use of antibiotics in various fields to prevent antibiotic resistance in new cases.[47]

PHARMACIST ROLE

In this study, Pharmacist should seek to increase our knowledge regarding the adverse effect and antibiotic resistance to the world wide population, constant and refreshing education of medical students, physicians and pharmacists is required. Regulation should be implemented with strict monitoring of antibiotic use as part of policy. Alternative to antibiotic such as probiotics and lytic bacteriophages can keep decreasing the burden of AMR globally. Further, pharmacist frequently collect and report data about interventions and antibiotic use patterns at hospital committee. In order to assess the effectiveness of the program, identify area for improvement and garner continued support for stewardship. Pharmacist are crucial to promoting currently available vaccines can decreases the use of antibiotics directly by preventing primary infection and Indirectly by preventing bacterial super infection after a primary vaccine- preventable illness such as influenza.[48] Communication between HCPs and their patients should play an important part in conveying correct usage of antibiotics to reduce ADR.[6]

10. CONCLUSION

Antibiotic crisis we have described how ADRs are predicted, prevented, detected and managed achieving the best outcomes from therapies remains a key goal because avoiding or mitigating the risk of ADRs (i.e: co-administration of other drugs monitoring, blood test results) continues to challenge everyday control the antibiotic resistance very difficult, but multipronged strategies should be adopted to confront this issue. At the national, regional, and global level, the tracking, bio-surveillance and response and prevention strategies of AMR and MDR pathogens may help to control the "global resistome".

Our study brings serious lapses in prescription pattern of antibiotics based on patient need and appropriate use of drugs. Most of antibiotics are prescribed with culture sensitivity test.

- Create an awareness based on the rational use of drugs.
- The antibiotic therapy should be given only after conducting a culture sensitivity test.
- The use of antibiotics as growth promoters should be prescribed.
- Use of narrow spectrum antibiotics is a first line therapy.[37]

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