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IATROGENESIS: AN OVERVIEW

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ABSTRACT

Iatrogenic disease is a clinical condition that is caused due to diagnostic, therapeutic, and prophylactic procedures undertaken on patients. These are unknown to physicians ranging from mild to severe. Risk factors related due to iatrogenic disease are the patient's age, diet, nutritional status, genetic variability, pre-existing pathology or comorbid conditions (especially of the kidneys and the liver), presence of the impaired host mechanism and drug sensitivity, etc. Iatrogenic diseases include ADR that is of 6 types – type A, type B, type C, Type D, type E, and type F. Types of drug-induced iatrogenic disease is antibiotic-induced, hypersensitivity, respiratory diseases, hepatic disease, and cardiovascular disease. Causes of iatrogenic disease are malpractice and medical error and negligence, overmedicalization of ill health, no prior warning about possible adverse drug reactions, and commercialization of medicine, it can be reduced at clinical and environmental levels.

KEYWORDS: Iatrogenesis, Drugs, Adverse drug reaction, Disease, Medical.

INTRODUCTION

Ivan Illich coined the term Iatrogenesis in sociology in 1976, declaring that modern societies impair quality of life by overuse of medicine.[1] This terminology was derived from the Greek word iatro-healer and genesis-origin. It means "brought forth by a healer", so it is the disease that is caused by the person who is supposed to be healing you. In the 19th century, it was seen that the transfer of pathogens take place from the autopsy room to the maternity room, leading to a shocking historical mortality rate due to puerperal fever, also known as childbed fever. It was a major iatrogenic disaster of era.[2-3]

According to World Health Organization (WHO), iatrogenesis is any noxious, undesired, unintended effect that occurs during prophylaxis, diagnosis, or treatment.[4] Iatrogenic diseases result from diagnostic, therapeutic, and prophylactic procedures on the patient that are unknown to physicians ranging from mild to severe.[5] In French general hospitals, the prevalence of community-acquired iatrogenic diseases is 2% to 10% and the prevalence of life-threatening complications due to iatrogenic diseases is 10% to 26%.[6] The risk factors for iatrogenic diseases are age, diet, nutritional status, genetic variability, preexisting pathology, impaired host mechanism, and Co-morbid condition of the liver and kidney.[7] The most important iatrogenic example is the teratogenic effects of thalidomide on the fetus of mothers who used thalidomide as a sedative and anti-nauseous.[8]

EXTENT OF IATROGENESIS:

The fifth leading cause of death in the world is iatrogenesis. Worldwide 5% to 8% of death take place due to ADRs. 5% to 10% of patients in developing countries may be affected by healthcare-associated infection.[9] worldwide unsafe injection practice (unsterilized syringes and needles) accounts for 40% of infection that leads to 1.3 million death each year.[10]

Although the Indian studies are very few, the patterns of iatrogenic disease are similar to that of western countries.[11] To assess the incidence, severity, pattern, causality, and predictability of ADRs and to identify risk factors for ADRs in highly active retroviral therapy, a study was conducted in India in 2010, where 130 retro-positive patients were monitored by active pharmacovigilance. 74 ADRs were identified from 57 patients. Anemia and hepatotoxicity were the most common ADRs.[12]

NATURE OF IATROGENESIS

Currently, thousands of medicines are being used and it is difficult to categorize ADR, there can be errors of omission, execution, and of planning. Classification of ADR is based on healthcare settings such as hospitals and nursing homes, the severity of resultant injuries can be near miss, no harm events, sentinel events, and legal implications of negligence.[13] ADRs can be classified as predictable such as toxicity, side effects, superinfection, and drug interaction, and unpredictable such as allergy, intolerance, pseudo allergy, and idiosyncrasy.[14] ADRs can be categorized based on reactions that occur in the administration of drugs. Type A(augmented)- depends on administered dose, severity increase with the dose. Type B(bizarre)-its reason is unknown, it cannot be predicted, and it may be fatal or serious. e.g. hepatitis is caused by halothane. Type C (continuous use of the drug)- is due to chronic

use of the drug. e.g. dementia occurs due to anticholinergic drugs. Type D (delayed)-It occurs when the treatment is stopped e.g. corneal opacity occurs after thioridazine. Type E (end of dose)- occurs on withdrawal of antidepressant drugs. Type F (failure of therapy) - occurs when there is a failure of treatment or treatment is ineffective.[15]

DRUG-INDUCED DISEASE

Iatrogenic diseases are the results of undesired effects of drugs, that leads to symptoms for which patient seek medical attention and/or hospitalization. Iatrogenic diseases occur due to impurities in drugs. A case of death due to contamination in heparin was reported in 2008. Strict monitoring by regulatory authorities, drug manufacturers, clinicians, and patients minimizes the harm that is caused by inappropriate drug use.[16]

When administered to the mother, drugs cause teratogenic effects on the fetus because these drugs cross placental barriers. Examples of Teratogenic drugs are alcohol, barbiturates, narcotics, and non-narcotics analgesic drugs like antihistamines, morphine, and tetracycline, secreted in milk so they should not be given to lactating mothers. Some drugs like hypnotics and tranquilizers have more effect on elderly patients. Drug-induced psychosis is also reported in some cases, which resolves in a few days.[17]

Table 1: SOME OF THE DRUGS AND THEIR INDUCED DISEASE.[18]

S. NO.	DRUG	DISEASE
1.	Cocaine	Heart, respiratory, nervous, and digestive disorders
2.	Inhalers	Heart failure, kidney, lung, and brain disease
3.	Opioid, anti-anxiety, sedative	Misuse of drugs can lead to death
4.	Heroin	Serious infectious disease
5.	Amphetamines	It can cause high body temperature, serious heart problems, and seizures
6.	MDMA(3,4-methylene-dioxy-methamphetamines)	Increase body temperature, heart rate, and blood pressure, toxic to nerve cells
7.	Nicotine	Cancer, emphysema, bronchial disorders, cardiovascular disease
8.	Steroids	Heart and liver disease, depression, stroke, and suicide
9.	LSD (Lysergic acid diethylamide)	Traumatic experience
10.	Marijuana	Tachycardia, psychosis
11.	Penicillin	Rash, diarrhea, hypersensitivity reactions
12.	Cephalosporins	Hypersensitivity reaction, serum sickness
13.	Aminoglycosides	Renal toxicity, ototoxicity, nausea/vomiting, dizziness, nystagmus
14.	Carbapenems	Diarrhea, headache, liver toxicity,

		eosinophilia
15.	Antitubercular agents	Diarrhea, anorexia, hemolytic anemia, liver toxicity, peripheral neuropathy
16.	Glycopeptides (vancomycin, telavancin)	Redman syndrome, phlebitis, taste alteration
17.	Macrolides	Abdominal pain, diarrhea, anorexia, nausea/vomiting, taste alteration
18.	Sulfonamides	Nausea/vomiting, diarrhea, anorexia, abdominal pain, headache, dizziness, rash
19.	Tetracyclines	Nausea/vomiting, diarrhea, abdominal pain, liver toxicity, photosensitivity reaction
20.	Quinolone (ciprofloxacin, levofloxacin, moxifloxacin, ofloxacin)	Lethargy, insomnia, diarrhea, photosensitivity.
21.	Lincomycin derivatives (clindamycin, lincomycin)	Pseudomembranous colitis, hypersensitivity reaction, jaundice
22.	Metronidazole	Nausea, vomiting, dizziness, headache, vaginal candidiasis
23.	cyclophosphamide	cystitis
24.	Methotrexate	Anemia
25.	Enoxaparin, tirofiban, paclitaxel, quinine	thrombocytopenia
26.	Anticancer Drugs	Bone marrow suppression
27.	Acetylsalicylic acid	hemolysis
28.	Steroids	osteoporosis
29.	Paclitaxel, Atorvastatin	Myalgia
30.	Methylprednisolone	Septic arthritis
31.	Carbimazole	Hypothyroidism
32.	Prednisolone	Cushing syndrome
33.	Risperidone	Obesity
34.	Olanzapine, steroids	Dyslipidemia
35.	Thyroid Hormone	Hyperthyroidism
36.	Deflazacort	Diabetes, menstrual dysfunction
37.	Hydroxychloroquine	Ocular toxicity
38.	Digitoxin	Arrhythmia
39.	Misoprostol	Menorrhagia
40.	Levofloxacin, co-trimoxazole	vasculitis
41.	Loperamide	Paralytic Ileus
42.	Carbamazepine	DRESS Syndrome
43.	Acyclovir	Oligospermia
44.	Steroids	Secondary infection
45.	Acetylsalicylic acid, Diclofenac	Gastritis
46.	Ibuprofen	Allergic Rhinitis
47.	Ceftriaxone, Azithromycin	Diarrhea
48.	Metoprolol, Diltiazem, Digitoxin	Bradycardia
49.	Diclofenac, Ibuprofen	Upper GI bleeding
50.	Methylprednisolone, levodopa	Psychosis
51.	Phenobarbitone, prednisolone	Cognitive dysfunction
52.	Metoclopramide, escitalopram	Extrapyramidal symptoms
53.	Steroids	Acne

54.	Sulfonamide	Serum sickness
55.	Ergot alkaloids	Unconsciousness, vision problems, convulsions

TYPES OF DRUG-INDUCED IATROGENIC DISEASES

1. Antibiotics-induced diseases

Antibiotics' most common side effects are allergies or hypersensitivity reactions that lead to emergency room admission. Drugs such as amoxicillin-clavulanate, ampicillin, and cefixime cause antibiotic-associated diarrhea.[19]

2. Hypersensitivity

In a small fraction of the population, allergic or hypersensitivity reactions are caused by particular drugs such as Penicillin, sulfonamide, phenacetin, etc. The most common drug allergic reactions are skin rashes, edema, anaphylactic shock, edema, bronchospasm, serum sickness syndrome, etc. Chronic use of aspirin causes salicylism.[20] Anaphylaxis is caused by drugs such as penicillin and other beta-lactam antibiotics, vaccines, sera, and human insulin. Non-IgE-mediated anaphylactic reactions are caused by aspirin and other NSAIDs (nonsteroidal anti-inflammatory agents).[21]

3. Respiratory diseases

Respiratory iatrogenic diseases are an important cause of morbidity and mortality. These Respiratory Diseases are caused by cytotoxic agents that include chemotherapeutic agents and noncytotoxic agents that are antibiotics, anti-inflammatory agents, and antiarrhythmics Nonspecific interstitial pneumonia (NSIP).[22] Hypersensitivity pulmonary Reactions are caused by drugs such as Nitrofurantoin, Busulfan, methysergide, Ganglion Blockers, and Sulfonamide.[23]

4. Hepatic Disease

Due to halothane, the intrinsic toxicity of drugs such as paracetamol and immune allergic mechanism causes liver damage. These liver diseases are usually reversible but chronic treatment leads to a progression of disease and liver cirrhosis.[24] Drug-induced hepatic diseases may occur as an idiosyncratic reaction to the nontoxic drug. These include both acute and chronic diseases. Acute injury includes hepatocellular or cholestatic jaundice. Chronic injuries contain a variety of hepatocellular, cholestatic, vascular, or neoplastic liver injuries, adverse effects of drugs, or injury to other organs.[25]

5. Cardiovascular Diseases

A heart patient takes an average of 6.8 prescribed medicines per day which leads to drug-drug interaction. NSAIDs can raise the chance of heart failure through water and salt retention. Thiazolidinediones lead to fluid retention and weight gain in patients with heart failure.[26]

CAUSES OF IATROGENESIS

A. Medical error and negligence

According to the WHO, a lack of qualified healthcare providers and incomplete knowledge about safe practices leads to major structural challenges. There is also an error in prescribing and delivering way of drug therapy to the patients. Accurate and timely diagnosis of the disease, management of preoperative care, and minimization of medication error are also other challenges to the health care system. The dearth of manpower in the healthcare system, directly and indirectly, leads to error. There is a deficit of doctors, nurses, and midwives in developing countries also contributes to an error.[10]

B. Malpractice

Health policies are also a major contributing factor to iatrogenic illness. For example, in the USA, due to practice of defensive medicine "occurs when doctors order tests procedures or visits or avoid certain high‐risk patients or procedures, primarily (but not necessarily solely) due to concern about malpractice liability.[27] Hence, doctors recommend medical examinations and medications to their patients indiscriminately. Fewer than 8% of all diagnostic tests are performed mainly due to fear of malpractice, according to the US office of technology.[28]

C. Overmedicalization of ill health

The autonomy of patients is compromised in dealing with their illnesses with modern medicine. The natural healing of disease is questioned by the medical sciences. The cultural way of managing an illness is not considered relevant anymore. Religious healing is rationalized. Various ways of traditional healing have been replaced by the over‐medicalization of ill health.[29]

D. No prior warning about possible adverse drug reactions

Warning about ADRs is unavailable in medical setting such as nursing homes, government hospitals, and clinics, the amount of risk is not communicated to the patient. In clinical trials or animal studies, ADRs are seen in later stages.[30]

E. Commercialization of medicine

Increased iatrogenesis is primarily due to the commercialization of medicines. Pharma companies declare their drugs as effective as they sponsor drug development and have tie‐ups with the petrochemical industry and financial companies as well.[31] These companies spend less on research and more on advertising. As a result, the actual efficacy and effectiveness of the medication are masked and side effects go unnoticed.[32]

HOW TO REDUCE IATROGENESIS

At the Clinical Trial level

At the clinical level, iatrogenesis can be reduced by improving the research base of drugs. The protocols have to be devised to increase the knowledge about medical errors, malpractices, And negligence. There is a need to learn from errors. Health care should raise the standard for improvement. There should be an organization inside the healthcare system to address the problem of ADRs.[33]

At the Environmental level

The determinants of disease are in the socio‐cultural environment. If there is an imbalance in the environment, shows its effects on the human organism. A healthy human organism depends on various aspects. Bio‐medicine defines treatment completely in bio‐physical terms, regarding cultural, and social factors.[34] Proper changes in the environment in terms of improving water quality, controlling vector-borne diseases, reducing air pollution, checking toxic chemical exposure, and improving nutrition can have a long‐lasting impact on the health of populations.[35]

CONCLUSION

The iatrogenic disease occurs due to drug reactions or the application of medical instruments to patients. It can also be due to an error in prescribing or delivering way of drug therapy to the patients. It is also due to the commercialization of medicines, which leads to the overuse of medications leading to the development of various adverse events like drug-drug interactions, anti-bacterial resistance, etc. At the level of clinical research, iatrogenesis can be reduced by improving the research base of drugs. At the societal level, iatrogenic diseases can be avoided by improving healthcare policies by healthcare policymakers and the appropriate use of drugs by healthcare professionals. It can also be reduced by proper application of medical instruments by paramedical staffs and educating patients for adhering to the prescriptions.

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