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Drug-Induced Diseases: A Comprehensive Review of Classification, Risk Factors, and Prevention Strategies

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Abstract: *Drug-induced diseases, called adverse drug reactions (ADRs), are defined by the World Health Organization as "any responses to a drug which are noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or the modification of physiological function" (1). ADRs are categorized into two types: Type A-reactions arising from augmented pharmacological effects and Type B-reactions arising from idiosyncratic effects (2). Drugs have the potential to inflict injuries on any organ and system, including but not limited to the liver, kidney, heart, and nervous system.*

Keywords: Drug-induced diseases

I. INTRODUCTION

Drug-induced diseases, called adverse drug reactions (ADRs), are defined by the World Health Organization as "any responses to a drug which are noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or the modification of physiological function" (1). ADRs are categorized into two types: Type A-reactions arising from augmented pharmacological effects and Type B-reactions arising from idiosyncratic effects (2). Drugs have the potential to inflict injuries on any organ and system, including but not limited to the liver, kidney, heart, and nervous system.

Drug-induced diseases, which are also referred to as adverse drug reactions (ADRs), imply unwanted reactions to drugs that lead to death or a condition with symptoms that are sufficiently severe to induce a patient to seek medical attention and/or require hospitalization (1). Such diseases could be triggered by different factors, including prescribed and over-the-counter drugs, herbal medications, and other substances (3).

Importance of recognizing drug-induced diseases

Recognition of drug-induced diseases is important as the major cause of morbidity and mortality in the world result from adverse drug reactions (ADR) [1]. ADRs relate severely to health consequences such as organ damage, disability, or even death [3]. According to World Health Organization estimates, about 10% of hospital admissions and 10-20% of hospital-acquired complication rates are due to ADR [1].

Economic Burden of ADRs

ADRs pose a significant economic burden at the level of individuals and society and ultimately at the level of nations, which could cost an average of $30-150 billion a year in the U.S. [4]. This economic burden includes the direct costs of ADRs, such as hospitalization, laboratory tests, and medication, together with indirect costs due to lost productivity and wages [5].

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Impact on Patient Outcomes

Enhancing the recognition of drug-induced diseases will improve patient outcome, as early detection and treatment can lessen the severity of ADRs and avoid long-standing damage [6]. The impact of ADRs on a patient is far-reaching, severely impeding their quality of life owing to pain, discomfort, and disability, which in turn translates into loss of productivity, increased use of health services, and compromised overall well-being [7].

Importance of Recognition for Patient Safety

Recognition of drug-induced diseases is vital for patient safety because this recognition allows health professionals to take measures that can prevent ADRs, such as monitoring patients for signs of ADR, altering medication regimens, or educating patients [8]. In this way, drug-induced diseases serve to mitigate the risks of ADRs, to the betterment of patient outcomes and patient safety in general [9].

II. CLASSIFICATION OF DRUG-INDUCED DISEASES

Drug-induced diseases can generally be classified into four types, such as Type A reactions, Type B reactions, Type C reactions, and Type D reactions. Each type has some characteristic effects and examples.

Type A Reactions

Type A reactions are those predictable, augmented pharmacological effects that largely depend on dose [2]. Type A reactions occur when therapeutic effects of a drug are exaggerated, with adverse consequences being given more emphasis.

Examples of Type A reactions include:

- Bleeding with anticoagulants: Anticoagulants increase the risk of bleeding because they impair blood clotting, e.g. warfarin [10].
- Hypoglycemia with insulin: Insulin can induce hypoglycemia (low blood sugar) on account of its metabolic effects on glucose [11].

Type B Reactions

Type B reactions are idiosyncratic reactions and unpredictable, having no dose dependency [2]. These reactions occur when a patient exhibits an abnormal or unusual reaction to a drug.

Examples of Type B reactions include:

- Stevens-Johnson syndrome induced by antibiotics: Stevens-Johnson syndrome is a rare, life-threatening skin and mucous membrane disorder that can be caused by certain antibiotics such as penicillin [12].
- Anaphylaxis with beta-lactam antibiotics: Beta-lactam antibiotics such as amoxicillin can cause anaphylaxis, a potentially life-threatening allergic reaction [13].

Type C Reactions

Type C reactions are dose- and time-dependent reactions occurring after prolonged use of a drug. They are also known as cumulative effects (2).

Examples of Type C reactions include:

- Hepatotoxicity with acetaminophen: Hepatotoxicity associated with acetaminophen occurs with very high doses and prolonged treatment [14].
- Nephrotoxicity with aminoglycosides: Aminoglycosides such as gentamicin can induce nephrotoxicity when used for long periods [15].

Type D reactions

Delayed Type reactions are those that occur when the drug has been withdrawn from the patient [2]. Such reactions are also termed 'late' reactions.

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Examples of Type D reactions are:- Antipsychotics and tardive dyskinesia: Tardive dyskinesia is a movement disorder that may develop after prolonged administration of antipsychotics such as haloperidol [16].
- Hydralazine and lupus-like syndrome: Long-term administration of hydralazine may produce a lupus-like syndrome, an autoimmune disorder [17].

III. ORGAN-SPECIFIC DRUG INDUCED DISEASES

These diseases may be induced by drugs in various organs and systems of the body. Here we discuss four organ-specific drug-induced diseases: hepatotoxicity, nephrotoxicity, cardiotoxicity, and neurotoxicity.

Hepatotoxicity

Hepatotoxicity can be defined as liver damage induced by drugs [18]. It has been known that the liver is a vital organ involved in the metabolism of drugs, and liver damage usually has severe consequences.
Some examples of drugs that may be hepatotoxic include:
- Acetaminophen, which is one among the commonly used over-the-counter analgesics [14]. It affects the liver when taken in large amounts or for long periods.
- Statins: Statins are cholesterol-lowering remedies that can cause hepatic injury in susceptible individuals [19].
- Antibiotics: Examples of antibiotics capable of promoting liver damage include erythromycin and rifampicin [20].

Nephrotoxicity

Nephrotoxicity is the condition of drugs acting on the kidneys [21]. The kidneys play a crucial role in filtering waste and toxins from the bloodstream. When drunkardic drugs or medications have elevated concentrations that injure kidneys, there can be a further decline in the functioning of these organ systems.
Examples of drugs that can induce nephrotoxicity include:
- NSAIDs: Injury to the kidney may occur with prolonged use of nonsteroidal anti-inflammatory drugs (NSAIDs), including ibuprofen and naproxen [22].
- Aminoglycosides: Gentamicin and tobramycin are examples of kidney-damaging antibiotic aminoglycosides [23].
- Contrast agents: Contrast agents used during imaging studies such as iodine and gadolinium may damage the kidneys in some patients [24].

Cardiotoxicity

Cardiotoxicity implies drug-induced harm to the heart [25]. The heart is a vital organ with the function of pumping blood to all parts of the body, and any damage inflicted on it can have dreadful consequences.
Some drug examples showing cardiotoxicity are: - Anthracyclines: Indeed, anthracyclines are chemotherapeutic agents, such as doxorubicin and daunorubicin, that can cause damage to heart [26].
- Beta blockers: The most efficacious beta blockers are propranolol and metoprolol. They are equally useful in regulating high blood pressure and heart problems, but in certain cases, they tend to be harmful to the heart [27].
- Anti-arrhythmic agents: These anti-arrhythmic agents include amiodarone as well as sotalol. They are used to treat irregular heartbeat but at times also can damage the heart of an individual [28].

Neurotoxicity

It defines nerve damage by drugs [29]. The control held over the different functions performed by the body by the central nervous system makes it a very critical component of the anatomy. The damage of nerves may lead to disastrous consequences.
Some of the examples of neurotoxic drugs are:
- Chemotherapy agents: Chemotherapy agents cause nerve damage; i.e. vincristine and cisplatin [30].
- Anticonvulsants: Anticonvulsants such as phenytoin and carbamazepine treat seizure but may cause nerve damage in some [31].

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- Local anesthetics: Local anesthetics, such as lidocaine and bupivacaine, may cause nerve damage as a result of incorrect use [32].

IV. SYSTEMIC DRUG-INDUCED DISEASES

A systemic drug-induced disease is defined as an adverse reaction at the level of drug interaction that affects several systems or organs of the body. We will discuss four types of systemic drug-induced diseases-allergic reactions, autoimmune reactions, endocrine disorder, and metabolic disorder.

Allergic Reactions

Allergic reactions to drugs can be either mild or serious to life-threatening [33]. In an allergic response, the substance is wrongly considered a harmful agent by the immune system, called an allergen, leading to the activation of an immune reaction against it.

Some examples of allergic reactions to drugs are:- Anaphylaxis: A severe, life-threatening allergic reaction occurring in a few seconds to minutes, may be the onset of respiratory distress, heart palpitations, and hypotension [34].

- Stevens-Johnson syndrome: A rare but deadly allergic reaction that brings about an eruption of blisters with peeling and desquamation of the skin [12].
- Drug rash: A common allergic reaction manifested by the symptoms of redness, itching, and blistering of the skin [35].

Autoimmune Reaction

Reactions that come as autoimmune reactions are immune system activations by different drugs that open up a variety of autoimmune disorders [36]. When an immune system identifies healthy tissues as foreign and mounts immune response against them, it is called an autoimmune reaction.

Here are a few types of drug-induced autoimmune reactions:

- Lupus-like reactions: Various autoimmune disorders that may cause manifestations such as joint pain, skin rash, and kidney damage [37].
- Rheumatoid arthritis: An autoimmune disease associated with symptoms of the joint, including pain, swelling, and stiffness [38].
- Thyroiditis: An autoimmunization with effects such as disease of the thyroid gland with inflammation, pain, swelling [39].

Endocrine Disorders

- Cushing's syndrome: A condition leading to hormone imbalance due to an overproduction of cortisol, which causes certain symptoms including weight gain, high blood pressure, and diabetes [40].
- Hypothyroidism: A hormonal disorder due to insufficient production of thyroid hormones thereby causing symptoms to include fatigue, weight gain, and dry skin [39].
- Hyperprolactinemia: A hormonal disorder caused by excessive secretion of prolactin leading to symptoms like infertility, galactorrhea, and amenorrhea [41].

Metabolic Disorders

- Hyperglycemia: A form of elevated blood glucose levels resulting from drugs like steroids, some antibiotics, and beta-blockers [42].
- Hypokalemia: Caused by lowpotassium levels as a result of using diuretics, certain antibiotics, and laxatives [43].
- Hyperlipidemia: Elevated cholesterol and triglyceride levels due to certain drugs like steroids, some antibiotics, and beta-blockers [44].

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V. RISK FACTORS FOR DRUG-INDUCED DISEASES INCLUDE:

1. Age

Adverse drug reactions are more common in elderly persons owing to age-related alterations in drug metabolism and excretion. The younger population is also at risk because of the development stage of their physiology [45].

2. Polypharmacy

Using many medications leads to the increased risk of adverse drug reactions. The most common interaction occurs when one drug interacts with another. For obvious reasons, the number and severity of the adverse drug reactions increase upon increasing the number of drugs taken [46].

3. Pre-existing Medical Conditions

Some pre-existing diseases are said to be risk factors in the occurrence of adverse drug reactions. For instance, a person suffering from liver and kidney diseases would be more at risk to some medications than others.

4. Genetic Predisposition

Variations in genetics can influence how specific medications interact with the body. Genetic polymorphisms concerning particular genes can lead to alterations in drug metabolism and a rise in drug levels, resulting in increased chances of an adverse drug reaction [47].

Other risk factors include:

- Pregnancy and breastfeeding: Increase risk; changed physiology and harm may be caused to fetus or baby
- Heredity: Genetic differences that affect drug metabolism
- Alcohol consumption: Increase the risks of adverse drug reactions
- Family history: Increased family history of substance use or misuse may put individuals at higher risk of adverse drug reactions.

To minimize adverse drug reactions, consider the following:

- Seek a consultation with a doctor or pharmacist to review medications and make adjustments as needed
- Monitor for possible side effects and report them to your healthcare provider
- Be aware of possible drug interactions with other substances, such as alcohol [46].

VI. PREVENTION AND MANAGEMENT OF DRUG-INDUCED DISEASES

Drug-induced diseases can be prevented and managed in a multi-faceted manner. They are:This entails monitoring medication use and side effects.

Monitoring each of these:

- Patient adherence to medication regimens
- Potential side effects and interactions
- Review and adjustments in treatment if indicated [48].

Dose Reduction

Dose adjustment strategies can include the following: changing the dose of drug to minimize side effects; increasing the dose gradually to achieve the required therapeutic effect; considering alternative dosing schedules or formulations [49].

Alternative

Preventive treatment for drug-induced diseases through alternative medications with a lower risk profile could be selecting fewer side effects or interactions; selecting medications with a low risk of toxicity or overdose; or using non-pharmacological treatments or modifications in lifestyle [50].

Education

Educate the patient of risks, benefits, and possible side effects in drug-included diseases. They include rights and obligations regarding [51].

VII. CONCLUSION

This review article is a compendious account of drug-induced diseases: the classification, organ specific and systemic effects, risk factors, prevention and management strategies.

The salient features include:

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- Drug-induced diseases can be of four types: Type A, Type B, Type C, and Type D reactions.
- Organ-specific drug-induced diseases include hepatotoxicity, nephrotoxicity, cardiotoxicity, and neurotoxicity.
- Systemic drug-induced diseases include allergic reactions, autoimmune reactions, endocrine disorders, and metabolic disorders.
- Risk factors for drug-induced diseases include age, polypharmacy, pre-existing illness, and genetic predisposition.
- Prevention and management strategies include monitoring, dose adjustment, alternative medications, and patient education.

Importance of Recognizing and Managing Drug-Induced Diseases

Recognition and proper management of drug-induced diseases can improve patient outcome and reduce costs. Knowledge of classification, risk factors, and prevention of drug-induced diseases can facilitate appropriate patient care, thereby minimizing the occurrence of adverse drug reactions by healthcare providers.

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