International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 1623-1629 www.ijprajournal.com ISSN: 2249-7781

Adverse Drug Reaction: A Review

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Submitted: 01-02-2023 Accepted: 10-02-2023

ABSTRACT: The term "side effects" also applies to negative medication reactions. Adverse drug reactions (ADRs) are harmful, unintended, and undesired effects that can arise from taking medications. These reactions happen as a result of self-medication or using prescription medications in excess. Adverse drug reactions can result from the prescribed drugs because they might also have unintended side effects. Most unfavourable medication responses can be avoided. Thus, one should only take medications that have been properly prescribed if they want to avoid having an unfavourable drug reaction. With the increased complexity of medication used to treat various diseases in an ageing society, ADRs are one of the rising causes of morbidity and mortality on a global scale and will continue to be a serious public health concern.

KEYWORDS: Side effects, Adverse Drug Reaction, Self-medication, Morbidity, Mortality.

I. INTRODUCTION

[1].ADRs, also known as ‘side effects’, ‘adverse drug events’, or ‘drug misadventure’, are a frequent cause of morbidity in hospital and the community. They have a significant cost both financially and in terms of quality of life.

[2].According to WHO ADR can be defined as 'any response to a drug which is noxious and unintended, and which occurs at doses used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function’.[3,4].ADRs could be a result of a preventable medication error, resulting in a side-effect as a result of medication administration, or an unforeseen error such as an allergic reaction.

[5].Adverse drug reactions (ADRs) are important. They should be considered in the differential diagnosis of a wide range of conditions, as any bodily system can be affected and any disease process mimicked. An adverse drug reaction is an unwanted or harmful reaction experienced after the administration of a drug or combination of drugs under normal conditions of use and suspected to be related to the drug.

[6].However, a variety of ADRs, including type A, type B, and type C adverse responses, have been recorded. Type A ADRs are frequently related to dose which enhance the normal therapeutic effect of drugs, with common reasons for overdose and alteration of the dose. While type B reactions have been described as idiosyncratic responses that are typically uncommon, unpredictable, and unrelated to the pharmacological actions of the drug, type C ADRs have been suggested to be connected with long-term drug therapies in which both serious and common effects on public health take place.

II. TYPES OF ADVERSE DRUG REACTIONS

[7].The most prominent pharmacological classification is the A(augmented or predictable) and B(augmented or predictable) classification, which is based mostly on how the adverse effects of the drug are considered to correlate to dose and mechanism.

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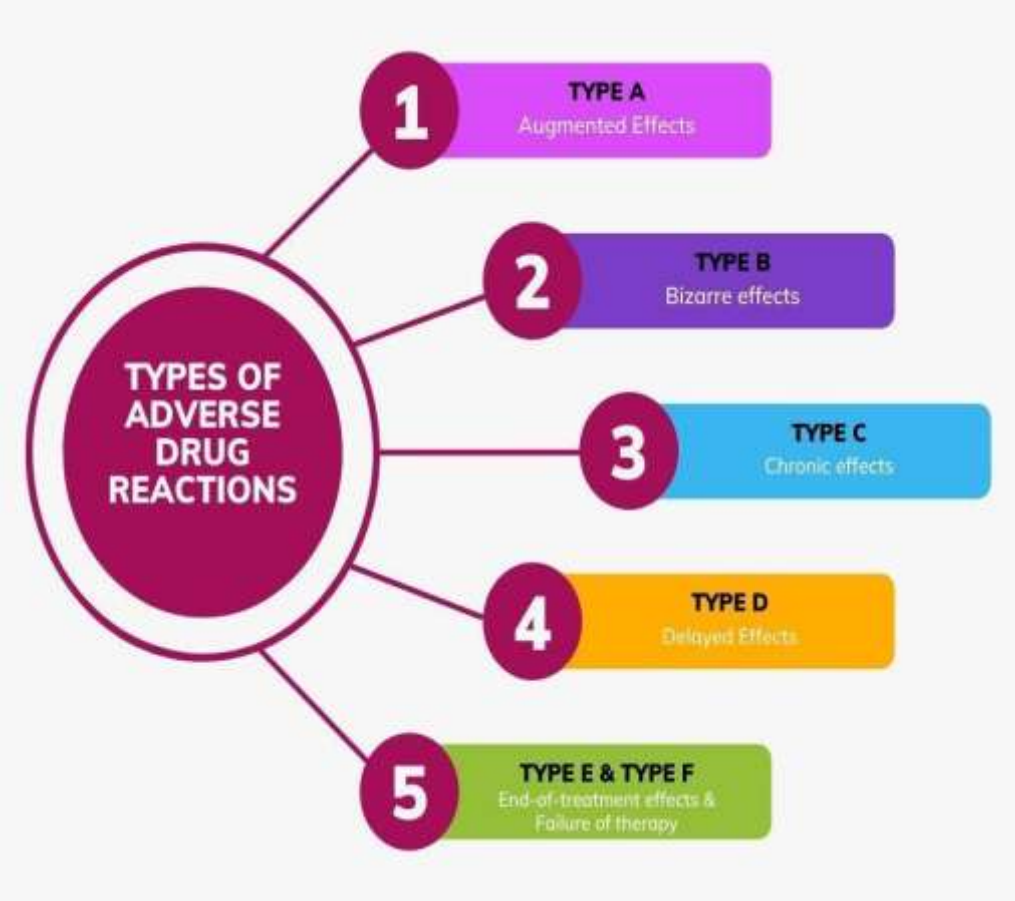

TYPES OF ADVERSE DRUG RECTIONS

Type A reactions

[8,10].An elevated but otherwise typical pharmaceutical effect. The following traits apply to type A reactions:

- mostly predictable
- often dose-dependent
- High incidence and morbidity
- Low mortality.

Type B reactions

[7,8,10,11].Idiosyncratic, aberrant, or bizarre drug effects that are unrelated to the pharmacology of the drug. The traits of type B reactions are as follows:

- Typically unpredictable
- Potentially missed by toxicological testing
- Not always dose-related
- Low incidence and mortality
- High mortality.

Type C reactions

[9,10].The type C adverse reactions have been linked to toxicities associated with chronic diseases that have substantial and widespread consequences on public health.

[11,12].Additionally, type C reactions have been defined as those that have chronic side effects brought on by long-term drug usage, such as extrapyramidal symptoms or analgesic nephropathy.

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Table 1: Pharmacological classification according to Hess and Rieder.

Predictable (Dose-dependent)	
Over dose	Toxic reaction to specific organ system due to excessive dose or impairedexcretion
Adverseeffects	Undesirable pharmacologic effects by mechanisms related to the desiredeffects
Drug-drug Interactions	Act ion of the drug on the effectiveness or toxicity of another drug
Drug-diseaseinteractions	Some disease processes interfere with metabolism or action of a drug
Unpredictable (Dose independent)	
Intolerance	Overstated, sometimes disabling effects even when the drug is given inusual doses
Idiosyncrasy	Abnormal reactions to a drug related to metabolic or enzyme deficiency which can be genetically determined, or altered activation/detoxificationpathways
Allergy	Reaction is specific to a given drug. Severe. Recurrent andlmmunolooicallv mediated
Pseudo Allergy	Clinically it is simiar to allergic reactions, but involves an unknownimmune mechanism

Table 2: Pharmacological classification according to Gharaibeh

Features	Type 1	Type 2
Synonyms	Augmented, predictable,toxic, quantitative, doserelated	Strange, unpredictable, idiosyncratic, Allergte, Drug intolerance, Dose
Mechanism	Understood,predictable	Generally poorly understood
Site	Some site of primary drug action Another site for primary and secondary actions	Usually the site of action is not related
Incidence	High (70%)	low (30%)
Morbidity	Mild	Severe
Mortality	low	High

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Table 3: Pharmacological classification according to Edwards and Aronson

Type	Characteristics	Action
A (augmented)	Pharmacological effectDose relatedFrequentPredictableLow mortality	Withdrawal orDose reduction
B (bizarre)	Rare Unpredictable Idiosyncratic High mortality	Withdrawal Avoid in the future
D (delayed)	Rare Mostly dose related,sometimes only after withdrawal	
E (end of use)	Rare or unpredictable,Rapid afterwithdrawal	Restart and tapering
F (failure)	Frequently Dose related; result ofinteractions	Dose increase effect co-medication
G (genetic)	Pharmacokinetic orPharmacodynamic	Doses adjustment or withdrawal and avoidance

DRUG INTERACTIONS

[19,20].Drug interactions occur when the effect of a drug is altered by the coadministration of any of the following:

- Another drug
- Food
- Drink.

The outcome of this is as follows:

- Frequently clinically insignificant
- Sometimes beneficial
- Occasionally potentially harmful.

MECHANISMS OF DRUG INTERACTIONS

[19,20].Interactions can be caused by pharmacokinetic (i.e., handling of the drugin the body is affected) or pharmacodynamic (i.e., related to the pharmacology of the drug) mechanisms. Sometimes the interaction can be causedby more than one mechanism, although usually one mechanism is moresignificant.

PREDICTING DRUG INTERACTIONS

- Are the desired or adverse effects of the two drugs similar oropposing?
- If there is no information available for the drugs in question, are therereports of drug interactions for other drugs in the same class?
- Are both drugs metabolized by the liver? If so, by which enzymes?
- Drugs that are predominantly renally cleared are unlikely to interactwith enzyme inducers and inhibitors.

MANAGING DRUG INTERACTIONS

- Check whether or not the drug combination is new.
- If the patient has already been taking the drug combination, has he or she tolerated it? If yes, there is probably no need to change therapy, although monitoring might be required.
- Is the interaction potentially serious?
- Remember that some drugs in the same class can have different potentials to cause interactions.

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- The elderly are at greater risk of drug interactions because of polypharmacy and impaired metabolism and excretion. Additive effects can be a particular problem in this population.
- Be aware of high-risk drugs and always check for potential interactions with these drugs.

III. MECHANISMS OFADVERSE DRUG REACTIONS

[13].An unpleasant and hazardous reaction brought on by an intervention after taking the medicine is known as an ADR. Direct toxicity studies and hypersensitivity reactions brought on by changes in the pharmacokinetic and pharmacodynamic properties of the drug products can be categorised under the mechanism of adverse reactions.

[14,15].The toxic effects of a substance or its metabolites, which manifest in different organ systems and cause undesirable chemical reactions, physiological dysfunction, DNA damage, or harm to cellular structures and tissues, may be responsible for direct toxicity reactions.

[16].On the other hand, hypersensitivity reactions, which include allergic and anaphylactic events, can be identified if the person's immune system exhibits an excessive response to a drug or its metabolites.

IV. DETECTION OF ADVERSE DRUG REACTIONS

[10,17,18].Since ADRs may act through the same physiological and pathological pathways as different diseases, they are difficult and sometimes impossible to distinguish. However, the following step-wise approach may be helpful in assessing possible drug-related ADRs:

- Ensure that the medicine received is the medicine ordered and actually taken by the patient at the dose advised.
- Verify that the onset of the suspected ADR was after the drug was taken, not before and discuss carefully the observation made by the patient.
- Determine the time interval between the beginning of drug treatment and the onset of the event.
- Evaluate the suspected ADR after discontinuing the drugs or reducing the dose and monitor the patient's status. If appropriate, restart the drug treatment and monitor recurrence of any adverse events.
- Analyse the alternative causes (other than the drug) that could, on their own, have caused the reaction, e.g. food.
- Use relevant up-to-date literature and personal experience as a health professional on drugs and their ADRs and verify if there are previous conclusive reports on this reaction. The National Pharmacovigilance Centre and Drug Information Centres are very important resources for obtaining information on ADR. The manufacturer of the drug can also be a resource to consult.
- Report any suspected ADR to the person nominated for ADR reporting in the hospital or directly to the National ADR Centre.
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V. REPORTING OF ADVERSE DRUG REACTION

[10,17,18].Most ADRs are not reported and this can lead to delays in identifying important reactions. The reasons for failure to report ADRs have been called the ‘seven deadly sins’:

- Complacency - a mistaken belief that only safe drugs are allowed onto the market and that these will not cause serious ADRs
- Fear - of involvement in litigation, or of a loss of patient confidence
- Guilt that a patient has been harmed by a prescribed treatment
- Ambition - to collect and publish a personal series of cases
- Ignorance - of what should be reported or how to make a report
- Diffidence - a reluctance to report an effect for which there is only a suspicion that it is drug related
- Lethargy - this may include a lack of time or interest, inability to find a report card, etc.

[10].The regulatory authorities in many countries have systems for reporting ADRs, and it is important to find out how ADRs are reported and whether pharmacists can submit reports. Institution-specifi c ADR programs may be developed to monitor, report, and prevent ADRs. Pharmacists are in an excellent position to oversee such programs.

VI. MANAGING ADVERSE DRUG REACTIONS

[8,10,13].Successful management of adverse drug reactions requires early identification and prompt treatment of anaphylaxis. To avoid inappropriately stopping necessary medicine, it is crucial to distinguish between symptoms unrelated

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to the drug and adverse drug reactions. When a therapy programme is introduced, good management also necessitates being aware of potential negative effects. Knowledge of suitable substitutes for these medications in the case of known hypersensitivity is beneficial, as is familiarity with the pharmacological groups most frequently responsible for immunologic responses. Using premedication measures as directed can frequently reduce the severity of an unpleasant reaction.

VII. CONCLUSION

Adverse drug responses are sometimes given insufficient consideration. They are frequent, potentially fatal, and needlessly expensive. By lessening the burden of drug toxicity, the actions listed in the box above are crucial for enhancing the benefit to risk ratio of pharmacological therapy. Because there are so many different medications out there, toxicity symptoms can take many different forms and have an impact on any organ system. In actuality, unfavourable reactions have surpassed syphilis and tuberculosis as the most effective imitators of other illnesses. The pattern of toxicity is likely to change with the introduction of new biotechnology products. Therefore, it is critical that prescribing clinicians are aware of the hazardous profile of the medications they prescribe and are constantly on the lookout for unexpected adverse reactions.

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