A Drug Use Mean Change in Human Body

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RESEARCH ARTICLE

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Abstract: A drug is any substance or combination of substances presented for the treatment or prevention of disease in humans or animals or any substance or combination of substances which may be administered to humans or animals for diagnosis or for performing, correcting, or modifying physiological function. The choice and administration of the drug are crucially influenced by its pharmacodynamic and pharmacokinetic properties. In addition to answering the question of what the drug does to the body, pharmacodynamics explains where and how the drug acts on the body.

Keywords: Drug, Pharmacology, Biotechnology, Therapy

Introduction

Pharmacology is the science that analyzes the interactions of substances with the human organism [1]. Pharmacodynamics describes the effects of substances on the organism, whereas pharmacokinetics analyzes the effects of the organism on substances and the path of drugs through the organism. Pharmacology is situated at the interface between physiology and pathophysiology. Pharmacology aims at curing diseases or at least mitigating disease symptoms on the basis of pathophysiologically validated concepts. For certain diseases such as hypertension, very effective and economical pharmacological treatments are available. In contrast, other diseases such as arrhythmias are much more difficult to treat pharmacologically. Accordingly, the focus for such diseases is to avoid their occurrence and particularly to avoid drugs causing arrhythmias.

Pharmacologically active substances are all chemical compounds that influence body functions. The term “pharmacologically active substance” makes no predictions about the benefit or harm of its effects. Drugs possess beneficial (therapeutic) effects, whereas poisons have deleterious (toxic) effects. The definition of a pharmacologically active substance as a drug or poison depends on the dose, mode of application, and the clinical situation.

Medicines are pharmaceutical preparations of drugs for use in humans. In addition to the drug, a medicine also contains pharmaceutical excipients that keep the drug in solution and accelerate or delay its absorption (controlled release formulations). Medicines can cause allergic reactions. Medicines comprise non-coated and coated tablets for oral administration, suppositories for rectal administration, transdermal systems for controlled release of a drug, and solutions for i.v., s.c., and i.m. injection, capsules for sublingual administration ensuring rapid systemic absorption and ointments, creams, eye drops, nose drops and sprays for local administration.

Medicines without the drug can exert therapeutic effects as well, specifically in situations with a psychological component. Such medicines are referred to as placebos. In headache, the response rate of placebos ranges between 30 and 70%, for GI disturbances between 20 and 60%, and for insomnia between 50 and 80%. The effects of placebos are due to the suggestive power of the physician, expectations of the patient, and behavioral conditioning. Placebos can also exhibit ADRs (nocebo effect). Sleepiness, abdominal pain, and headache are typical nocebo effects and occur in up to 50% of all patients treated with placebos.

Biotechology

The field of pharmaceutical biotechnology represents the marriage of many scientific specialties including genomics, proteomics, personalized medicine, drug discovery and development, lab-on-a-chip microtechnology, nanomedicine, and more [2]. Scientists doing research in pharmaceutical biotechnology are focused on increasing the effectiveness of the drug treatments while minimizing potentially serious side effects. Pharmaceutical biotechnology research also focuses on developing new medicines and therapies to treat diseases in humans. Access to the complete DNA sequence of the human genome, including the continual sequence corrections and updates, provides a powerful resource that offers scientists a much more detailed picture of how human cells work and what goes wrong when disease strikes.

Scientists must have a detailed understanding of the intricate processes inside the cell in order to design drugs that can

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function along with normal bodily activities and also kills pathogens, often in the same cells. This information is essential for research in pharmaceutical biotechnology. Inside the human body, pharmaceutical drugs must maintain a fine balance between offering an effective treatment for a disease while at the same time avoiding potentially serious side effects. The most effective medications are drugs that do not interact with most cellular components while successfully attacking the intended target molecules that cause the disease.

Products

Pharmaceutical products play a central role in the prevention and treatment of disease [3]. Making safe and effective pharmaceutical products available and affordable to individuals around the world is a central challenge to the global governance system. There are however myriad obstacles to achieving and maintaining effective worldwide availability of medicines.

Despite the fact that people around the world face largely similar challenges from disease, the policy framework for promoting innovation and regulating pharmaceutical supply is remarkably disjointed. Innovation policy, insofar as it is implemented at all, is established on a country-to-country basis with minimal attention to the coordination of research and development. Regulatory structures are almost equally fragmented. Each country has its own set of approval standards and regulatory procedures that must be dealt with, and only to a limited extent are there cooperative procedures or systems of mutual recognition. Corporate decisions concerning where to concentrate on innovative efforts, what to produce, where to supply it, and on what terms are based on the likely impact on profits and capital markets.

There are wide disparities in levels of income both among countries and within countries. Prices that are reasonably affordable for individuals covered by health insurance in developed countries are likely to be unaffordable for individuals without health insurance in developed and developing countries. There are compelling needs for new medicines to treat diseases affecting both the rich and poor, such as diabetes, cancer, heart disease, and the degenerative disorders of old age. Innovation in these areas is costly, yet even with substantial sums invested in research and development rates of innovation are surprisingly low. There are equally compelling needs for new medicines to treat disease conditions predominantly afflicting tropical regions where poverty rates are typically high. Far less is invested in the diseases of the poor because of a lack of market demand.

Drug

In the most general sense, a drug may be defined as any substance that brings about a change in biological function through its chemical actions [4]. In most cases, the drug molecule interacts as an agonist (activator) or antagonist (inhibitor) with a specific target molecule that plays a regulatory role in the biologic system. This target molecule is called a receptor. In a very small number of cases, drugs are known as chemical antagonists may interact directly with other drugs, whereas a few drugs (osmotic agents) interact almost exclusively with water molecules. Drugs may be synthesized within the body (eg, hormones) or maybe chemicals not synthesized in the body (ie, xenobiotics). Poisons are drugs that have almost exclusively harmful effects. However, Paracelsus (1493–1541) famously stated that “the dose makes the poison,” meaning that any substance can be harmful if taken in the wrong dosage. Toxins are usually defined as poisons of biologic origin, ie, synthesized by plants or animals, in contrast to inorganic poisons such as lead and arsenic.

To interact chemically with its receptor, a drug molecule must have the appropriate size, electrical charge, shape, and atomic composition. Furthermore, a drug is often administered at a location distant from its intended site of action, eg, a pill given orally to relieve a headache. Therefore, a useful drug must have the necessary properties to be transported from its site of administration to its site of action. Finally, a practical drug should be inactivated or excreted from the body at a reasonable rate so that its actions will be of appropriate duration.

SUD

Pharmacotherapy for substance use disorders (SUDs) may include interventions to assist with recovery from an overdose, detoxification, and relapse prevention [5]. Multiple medications have been identified as potential treatments to help patients who suffer from an SUD. As a result, much research has been conducted to test the efficacy of these interventions. Unfortunately, many factors create burdens for researchers attempting to conduct pharmacotherapy trials with this population. For example, researchers may experience challenges in recruiting appropriate participants, achieving randomized double-blind conditions, limiting treatment non-adherence and drop-out, selecting adequate outcome measures, and preventing safety concerns. These difficulties can negatively affect the reliability, validity, and generalizability of study results. As a result, many contradictory findings have been published, and the field still awaits the discovery of medications that will assist individuals recovering from various substances of abuse. However, advances in pharmacological treatment have revolutionized clinical care for patients with SUDs, and many individuals are able to achieve stable recovery and lead productive lives.

In addition to providing life-saving treatment, psychopharmacological interventions can aid significantly in the detoxification process for individuals with substance dependence. For some users, detoxification is the most difficult component of addiction treatment, due to the highly aversive physical or psychological symptoms associated with withdrawal from the substance of abuse. Effects caused by

sudden detoxification can range from discomfort to fatality. In the case of alcohol detoxification, results of pharmacological trials have demonstrated benzodiazepines to be the safest and most efficient medications for the treatment of withdrawal symptoms by chemically 'imitating' alcohol's effects on the brain gamma-aminobutyric acid (GABA-A) receptors. In addition to benzodiazepines, one study has shown that treatment with clomethiazole during alcohol detoxification may reduce risks of premature discharge among inpatients.

Opiate detoxification is an especially difficult process, and pharmacotherapy is used in the majority of inpatient cases. Results of pharmacotherapy trials have shown the most effective treatment to be substituting and tapering methadone or buprenorphine. In addition, for patients with polysubstance dependence, research has demonstrated that a combination of buprenorphine and valproate is a safe and effective option for the treatment of a variety of withdrawal symptoms. For some patients, long-term treatment (i.e. maintenance therapy) with methadone, buprenorphine, or other medications may allow them to avoid withdrawal symptoms while abstaining from the drug of abuse.

Pharmacological Factors

It is important to note that, whatever the level of use, drugs affect different people in different ways [6]. The effects that a psychoactive substance or 'drug experience' will have on a given individual will depend on several other factors besides the pharmacological properties of the drug, such as the set and the setting. The set is the personality or the psychological state an individual brings to the experience, like thoughts, mood or expectations. The setting refers to the context of the physical or social environment.

The pharmacological factors include the chemical properties or type of drug used. Different drugs have a different modes of action on the body due to their pharmacological properties; also important is the purity and strength of the drug, the route of administration, and whether it is used in combination with other drugs. In addition, the effects or actions of a psychoactive drug are influenced by the personal characteristics of the drug user. These characteristics include factors such as the person's biological make-up, personality, gender, age, and drug tolerance, and the user's previous experience of the drug. The psychological state of the individual is also relevant, for example, those with low mood or who are anxious or depressed are more liable to have disturbing experiences when using psychoactive substances. Health problems such as cardiovascular disease, hypertension, asthma, epilepsy, diabetes mellitus, or liver disease can exacerbate the use of psychoactive substances and make them more unsafe. The last set of factors to be considered is the setting or context in which a drug is used. This includes the physical environment where the drug is used, the cultural influences of the community where the drug is consumed, the laws relating to drug use, and the context in which a drug is used. It is stated that 'it is necessary to see the drug – brain interaction not as a simple chemical event but as a matter of considerable complexity involving the drug, the particular person, and the messages and teachings which come from the environment and which powerfully influence the nature and meaning of the drug experience'.

Biomarkers

Biomarkers are typically used to define the onset, continuation, and either positive or negative characteristics of the induced biological effects of the drug (chemical) under research [7]. Biomarkers have been classified as biomarkers of exposure, susceptibility, and outcome. The definition of a biomarker as used in drug discovery and development is a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic response(s) to a therapeutic intervention. In pharmacological studies, where a relevant therapeutic target is identified and pursued, biomarkers are developed that correlate with the proof of concept for the drug candidate. Biomarkers are developed to show (1) that a desired modulation of the target occurs as anticipated by the chemical therapeutic; (2) that the chemical-induced target modulation produces a desired biological effect; (3) that the induced biological effect alters the disease under study; and (4) that there may be increased susceptibility to the therapeutic candidate by certain individuals, such as those based on pharmacogenetic predispositions. In toxicology studies, biomarkers are objectively measured and evaluated as indicators of (1) normal biological processes; (2) pathogenic processes; (3) pharmacologic response(s) to a therapeutic intervention, which in some cases could mean excessive or nonspecific pharmacologic activity; and (4) exposure-response relationships. Pharmacogenetic markers are also studied from a toxicological standpoint, particularly in relation to drug metabolism. In environmental research and risk assessment, biomarkers are frequently referred to as indicators of human or environmental hazards. Discovering and implementing new biomarkers for toxicity caused by exposure to a chemical from a therapeutic intervention or in some cases through unintentional exposure continues to be pursued through the use of animal models to predict potential human effects, from human studies (clinical or epidemiological) or from biobanked human tissue samples, or the combination of these approaches. In addition, several omics technologies such as transcriptomics, metabolomics, and proteomics have added an important aspect to biomarker research.

Therapy

It is self-evident that the benefits of drug therapy should outweigh the risks [8]. Benefits fall into two broad categories: those designed to alleviate a symptom, and those designed to prolong useful life. An increasing emphasis on the principles of evidence-based medicine and techniques such as large clinical trials and meta-analyses have defined the benefits of

drug therapy in specific patient subgroups. Establishing the balance between risk and benefit is not always simple: for example, therapies that provide symptomatic benefits but shorten life may be entertained in patients with serious and highly symptomatic diseases such as heart failure or cancer. These decisions illustrate the continuing highly personal nature of the relationship between the prescriber and the patient.

Some adverse effects are so common, and so readily associated with drug therapy, that they are identified very early during clinical use of a drug. On the other hand, serious adverse effects may be sufficiently uncommon that they escape detection for many years after a drug begins to be widely used. The issue of how to identify rare but serious adverse effects (that can profoundly affect the benefit-risk perception in an individual patient) has not been satisfactorily resolved. Potential approaches range from an increased understanding of the molecular and genetic basis of variability in drug actions to expanded postmarketing surveillance mechanisms. None of these have been completely effective, so practitioners must be continuously vigilant to the possibility that unusual symptoms may be related to specific drugs or combinations of drugs, that their patients receive.

Beneficial and adverse reactions to drug therapy can be described by a series of dose-response relations. Well-tolerated drugs demonstrate a wide margin, termed the therapeutic ratio, therapeutic index, or therapeutic window, between the doses required to produce a therapeutic effect and those producing toxicity. In cases where there is a similar relationship between plasma drug concentration and effects, monitoring plasma concentrations can be a highly effective aid in managing drug therapy, by enabling concentrations to be maintained above the minimum required to produce an effect and below the concentration range likely to produce toxicity.

Pharmacovigilance

Pharmacovigilance consists of the continual collection, review, and analysis of adverse reactions (ADRs) to a medicinal product [9]. This involves the spontaneous reports received by a pharmaceutical company from doctors, healthcare workers, and patients and also may involve formal studies of medicine adverse reactions. ADRs are notoriously under-reported by healthcare workers and hence pharmacovigilance studies may be necessary.

Pharmacovigilance studies are sometimes classified as phase 4 trials but are more appropriately called post-marketing surveillance studies. These are non-interventional and essentially observational with the aim of gathering more safety data about newly licensed medicine. Various techniques can be used to gather such data such as cohort studies, case-control studies, and computerized databases which link prescriptions to ADRs. On average when a new medicine is licensed about 1500-3000 humans will have been exposed to it. If a particularly adverse reaction to this new medicine only occurs in 1 in 5000 patients, then it is obvious that the pre-licensing data has little chance of detecting this. Hence pharmacovigilance is only beginning when a medicine reaches the market.

There are well-known examples of medicines which were withdrawn from the market place when previously unknown adverse reactions became apparent. It is in the best interests of any company that they should learn of any safety issues as soon as possible so they may react accordingly. For example, it may be discovered that the product interacts with another medicine or that the dose needs to be carefully monitored in a certain group of patients (the elderly, those with liver failure, etc.). The company will want to protect patients from any harm, will want to further investigate the problem, and will want to issue any warnings that are appropriate.

Quality Control

A pharmaceutical industry quality control laboratory has the important function of testing raw materials, packaging components, materials being processed and finished products for quality [10]. It is important to recognize that quality control plays an important role in the quality assurance of pharmaceuticals all the way from research and development on investigational medicinal products, through to scale-up and commercial manufacture. Key decisions are made from the analytical data generated and so the reliability of the results is paramount. The safety of patients depends upon the body of knowledge generated by analytical chemists on active pharmaceutical ingredients (APIs) and drug products during product research and development, process validation studies, stability testing, in-process control and finished product testing. When problems occur, the data generated by the quality control laboratory will help to determine the root cause and improve process and product quality.

Testing laboratories involved in the generation of data for product development, marketing authorization, and batch release of medicinal products face the challenge of undertaking their activities in a heavily regulated environment. In addition, as a functional and costly part of the business, testing laboratories must run their operations as efficiently as possible.

Regulatory authorities such as the Medicines and Healthcare products Regulatory Agency (MHRA), the Food and Drug Administration (FDA) or the European Agency for the Evaluation of Medicinal Products (EMEA) enforce national and international regulations. In order to comply with these, pharmaceutical companies are required to put appropriate quality systems in place. Maintaining the quality system in good working order draws heavily on resources, and costs can be high. Regulatory compliance versus lean and efficient operational costs can be the dichotomy that every manufacturer faces.

Conclusion

Two or more drugs taken in the same period can cause both beneficial and adverse effects by their interaction; thus it can facilitate treatment or increase the frequency and severity of side effects. Interactions occur not only on prescription drugs but also on over-the-counter drugs. If someone is being run by more than one doctor, each of them needs to know what all medications the patient is already receiving. It is best to pick up all medicines in the same pharmacy, especially if there are records of dispensed preparations. Then the pharmacist can easily check the likelihood of certain interactions. The same consultation is required when taking over-the-counter medications, especially if medications prescribed by a doctor are taken at the same time.

References

1. Seifert, R. (2019.): „Basic Knowledge of Pharmacology“, Springer Nature Switzerland AG, Cham, Switzerland, pp. 5.
2. Fitzgerald-Hayes, M.; Reichsman, F. (2010.): „DNA And Biotechnology, Third Edition“, Academic Press, Elsevier, Burlington, USA, pp. 288.
3. Abbott, F. M.; Dukes, G. (2009.): „Global Pharmaceutical Policy - Ensuring Medicines For Tomorrow's World“, Edward Elgar Publishing Limited, Cheltenham, UK, pp. 1.
4. Katzung, B. G. (2018.): „Introduction: The Nature of Drugs & Drug Development & Regulation“ in Katzung, B. G. (ed): „Basic & Clinical Pharmacology, 14th Edition“, McGraw-Hill Education, New York, USA, pp. 3.
5. Merlo, L. J.; Arana, J.; Stone, A. M. (2010.): „Pharmacological Trials for the Treatment of Substance Use Disorders“ in Hertzman, M.; Adler, L. (eds): „Clinical Trials In Psychopharmacology - A Better Brain, Second Edition“, John Wiley & Sons, Ltd, Chichester, UK, pp. 207. – 218.
6. Rassool, G. H. (2010.): „Addiction for Nurses“, Wiley-Blackwell, John Wiley & Sons Ltd, Chichester, UK, pp. 41. – 42.
7. Johnson, D. E. (2017.): „Systems Biology Approaches in Pharmacology and Toxicology“ in Johnson, D. E.; Richardson, R. J. (eds): „ Computational Systems Pharmacology and Toxicology“, The Royal Society of Chemistry, London, UK, pp. 8.
8. Roden, D. M. (2005.): „Principles of Clinical Pharmacology“ in Kasper, D. L.; Braunwald, E.; Fauci, A. S.; Hauser, S. L.; Longo, D. L.; Jameson, J. L. (eds): „Harrison's Principles of Internal Medicine, 16th Edition“, The McGraw-Hill Companies, Inc., New York, USA, pp. 13.
9. Stinson, J. C. (1999.): „The develompent of new medicines: an overview“ in Walsh, G.; Murphy, B. (eds): „Biopharmaceuticals, an Industrial Perspective“, Kluwer Academic Publishers, Dordrecht, The Netherlands, pp. 285.
10. Graham, P. (2011.): „Quality Control in the Pharmaceutical Industry“ in Moffat, A. C.; Osselton, M. D.; Widdop, B. (eds): „Clarke's Analysis Of Drugs And Poisons“, Pharmaceutical Press, London, UK, pp. 350.