Drug utilization studies

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INTRODUCTION

Drug utilization studies are a prerequisite for the formulation of drug policies. They also offer useful methods for teaching and training in drug therapy. It is well known that indiscriminate use of drugs results in unwanted side effects, drug interactions and ecological disturbances and poses difficulties in diagnosis. Problems such as improper storage, distribution, compliance and selection of drugs constitute a major threat to society. Drug catastrophes and addiction are serious issues of the day. Manufacturers create artificial demands of unwanted drugs and drug combinations through competitive sales promotions. Most of these drugs are accepted by prescribing physicians without full knowledge of their cost, efficacy and safety. This review identifies the problems that arise from drug usage in the health care delivery system and highlights the current approaches to the rational use of drugs.

A meeting of the WHO Drug Utilization Research Group (DURG) was held in Cologne, Federal Republic of Germany, in November 1985, to discuss the results of current research and to set priorities for future activities.[1] In 1986, the WHO collaborating centre for Drug Statistics Methodology, Oslo, Norway, published the *Drug Utilization Bibliography*[2] which contains a list of 709 papers published between May 1981 and January 1986. At about the same time, the WHO International Monitoring Centre at Uppsala was entrusted with the task of coordinating the research on drug utilization in various countries. It is worth noting that the Nordic countries pioneered drug utilization studies and have reported interesting facts about the pattern of drug usage.[3–5]

OBJECTIVES

It is believed that the use of drugs is dependent mostly on the personalities of the prescriber and the patient. Even then, drugs are not used to their full potential or according to conventionally accepted criteria. Drug utilization studies provide data on prescribing patterns and may help improve the prescribing habits of general medical practitioners. Some basic objectives of drug utilization studies are as follows:

(1) Identify good and bad prescribing practices
(2) Encourage rational prescribing
(3) Provide guidance to help solve problems associated with drug therapy
(4) Assess the therapeutic, toxic and economic aspects of drugs and their combinations
(5) Inform various authorities about drug-related offences
(6) Critically analyse drug utilization and help frame a drug or health policy.

DEFINITION

Drug utilization has been defined by the WHO as the study of the marketing, distribution, prescription and use of drugs in a society with special emphasis on the resulting medical, social and economic consequences.[6] Some of the potential consequences of drug utilization are listed in Table I.[7]

TABLE I. Consequences of drug utilization

Medical	
Benefits	Efficacy in preventing, relieving and curing diseases of their complications and symptoms
Risks	Short term and long term adverse effects
Special risk factors	Genetics, disease, environment, nutrition, age, sex, pregnancy, lactation, etc.
Inappropriate prescription and use enhance the risks and reduce the benefits	
Social	Current trends in drug and health attitudes
	Drug abuse and dependence
	Misuse of drugs (non-compliance, selection of inappropriate drugs for the purpose)
	Discrimination and social injustice (important drugs not available)
Economical	Drug cost (local production versus import)
	Health economy (cost effectiveness of drugs)
	National resources (money, manpower, competence and facilities) for the drug and health budgets

FACTORS INFLUENCING DRUG UTILIZATION

Various factors influence drug utilization patterns (Table II). Properly conducted studies are invaluable tools for decision-making in drug and health policies. They also represent a mechanism for improved communication between health authorities, scientists and health personnel.[8]

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TABLE II. Factors influencing drug utilization

1.	Scientific and technological achievements and priorities
2.	Medical needs and demands (morbidity and expectations)
3.	Structure and organization of the health services (goals and ambitions)
4.	General economy (cost of the drug)
5.	Regulatory efforts (national drug policies)
6.	Promotion by the drug industry (drug development and production)
7.	Efforts to inform by independent sources
8.	Professional and public preferences
9.	Socio-demographic, geographical, cultural and traditional factors
10.	Others, e.g. lay press, mass media

USES

The WHO has recommended that more recognition and support should be given to Drug Utilization Studies and related work and governments should be made aware of the importance of such studies.[1] The studies should be conducted in collaboration with professionals such as clinical pharmacologists, physicians, pharmacists, health economists and epidemiologists. Drug usage figures should form an integral part of national statistics and should be made accessible to research workers and health planners. Such data should be used to:

(1) describe patterns of drug use at various levels of the health care system, monitor periodically the development of therapeutic profiles and make estimates of the number of patients exposed to various drugs.
(2) measure the effects of educational, informative and regulatory efforts and price policies, thus providing a basis for adjustments whenever necessary.
(3) define areas for further investigations on the absolute and relative efficacy and safety of drug therapy.
(4) help determine comparative costs and benefits.
(5) indicate the overuse, underuse or misuse of individual drugs or therapeutic classes.
(6) estimate drug needs in relation to morbidity patterns, to provide a basis for drug selection, supply, distribution and use as part of a drug and health policy.

STRATEGY

The Nordic countries[8] and the WHO Drug Utilization Research Group (DURG) suggested a strategy of step-wise events by which single drug or drug products could be studied. The full implementation of such a system is summarized in Table III.

TABLE III. Step-wise flow chart for drug utilization studies

1.	Description of drug and cost profiles according to population exposure, administrative area, socio-demographic factors, etc.
2.	Preliminary data analyses and interpretation. Identification of the problem and its relevance and importance
3.	Supplementary studies of various types such as drug prescription and use and recording of therapeutic and adverse effects
4.	Data analyses and interpretation, and tentative conclusions
5.	Feedback from professionals. Educational, informative or regulatory measures to promote more rationalized drug therapy

METHODOLOGY

Even though the basic methodology involved in drug utilization studies is complex, it may be simplified for general medical readers. First of all, drugs can be classified and coded. Secondly, the information regarding the cost or quantity of drugs can be obtained from various sources such as manufacturers, prescribers or users. Thirdly, it is possible to estimate the prevalence of drugs in a community. Some of the procedures adopted for the overuse, underuse or misuse of drugs are given below.

Anatomical–Therapeutic–Chemical Classification Code

No drug classification system is perfect when viewed in totality of epidemiological, pharmacological, pharmaceutical and chemical aspects. However, the European Pharmaceutical Market Research Association (EPHMRA) and the International Pharmaceutical Market Research Group (IPMRG) have developed an Anatomical–Therapeutic–Chemical (ATC) classification code.[3–5,8] According to the ATC system, all drugs are divided into 14 main classes which are subdivided into levels of five more subgroups (Table IV). The WHO-DURG and the Nordic countries have adopted the ATC code.

TABLE IV. ATC code drug classification system

Fourteen main drug classes:

A	Alimentary tract	L	Cytostatics
B	Blood and blood forming organs	M	Musculo-skeletal system
C	Cardiovascular system	N	Central nervous system
D	Dermatological preparations	P	Parasitology
G	Genito-urinary and sex hormones	R	Respiratory system
H	Systemic hormonal preparations	S	Sensory organs
J	General anti-infectives	V	Various others

Example: ATC coding of diazepam = N 05 B A 01

N	Central nervous system	main class
05	Psycholeptics	therapeutic subgroup
B	Tranquillizers	therapeutic subgroup
A	Benzodiazepines	chemical subgroup
01	Diazepam	chemical substance

Units of Measurement

For comparative studies units of measurements could either be the cost or the quality of a drug. Cost may be defined in terms of overall cost of therapy, package, dose or regimen; quantity may be calculated in terms of number of tablets, vials, packages or prescriptions. Information may be obtained from patients, physicians, hospitals, health insurance systems and pharmacists or from market surveys. Comparison may be made between different countries and regions.[8,9]

The Defined Daily Dose Concept

The defined daily dose (DDD) concept represents a method for the quantification of drugs. The DDD of a drug refers to the assumed daily dose in adults for its main indication. Sales or prescription data compiled and

TABLE V. Example of defined daily dose (DDD) for anti-diabetic drugs (as adopted in Norway)

Parenteral preparations	
Insulin (various formulations)	40 i.u.
Oral preparations	
Biguanide derivatives	
Metformin	2 g
Phenformin*	0.1 g
Sulphonamide derivatives	
Chlorpropamide	0.375 g
Glibenclamide	10 mg
Glymide	1 g
Glibornuride	38 mg
Tolbutamide	1.5 g

*Discontinued in Norway after 1976

presented as number of DDDs per 1000 inhabitants per day may provide a rough estimate of drug exposure within a community (Table V).[3,4,5,9,10]

Operation Research Group in India

In India, the Operation Research Group, Baroda, has made a sample survey of drug sales in 1985–86.[11] They have analysed the data using an anatomical classification of drugs.

DISCUSSION

Drug Market

The drug market is very dynamic, continuous and rapidly changing. Its salient features are:[3,12–15]

(1) New drugs or drug products are continuously introduced to the market.
(2) New drugs are assumed to be better than old drugs but are generally more expensive and add substantially to the rising drug bill.
(3) Prescribers quickly accept newer drugs.
(4) It is estimated that between 14% and 20% of all drug sales is spent on sales promotion such as organization of meetings and symposia (including wining and dining) and marketing trials of new drugs.
(5) The market is influenced by import and export of bulk drugs and final products, causing much competition among drug manufacturers.
(6) The unacceptable pharmaceutical products of the western society are marketed in developing countries. This is commonly known as 'drug dumping'.
(7) The drug companies have a tendency to combine drugs. There are about 50 000 brand preparations of drug combinations in the Federal Republic of Germany and 30 000 combinations in the USA for less than 2000 single drugs, whereas the WHO has recommended only 9 fixed dose combinations. Similarly, there are about 25 000 drug formulations on sale in India.
(8) The vast majority of combined drugs are sold at prices higher than the combined value of the ingredients. Very often such combinations are useless and superfluous; at times they are positively harmful.
(9) Critics of the medical profession are aware that producer-independent information and evaluation are essential facts regarding the therapeutic status of a drug.

The Essential Drugs Model List

To overcome the complication of drug selection, the WHO has prepared a model list of essential drugs on the basis of current scientific information.[6,16] The listed drugs are the ones most needed to satisfy the health needs of most of the population. Such drugs should be always available in sufficient quantity and in appropriate dosage. Where two or more drugs appear to be approximately similar, the choice should be based on a careful evaluation of their relative efficacy, safety, quality, price and availability. The WHO list is intended to serve as a guideline to assist other countries in preparing their own lists depending on their individual morbidity pattern, health priority and economic system. In 1982 Bangladesh adopted an essential drugs list of 250 single agents of which 42 are meant for primary health care.

Cost of Drugs

Total world production of drugs is valued at around US $100 billion of which 85% is consumed by developed nations. The remaining 15% is available to two-thirds of the world's population living in developing countries.[12]

In 1982, hospitals in the USA spent about 3 billion dollars on drugs and a third of this was for systemic anti-infectives.[17] It is stated that drugs cost far more than the cost of keeping a patient in hospital.[18] In India very few studies have been conducted to estimate drug costs. However, it has been shown that the largest amount of money (39%) is spent on chemotherapeutic agents.[13]

Prescribing Errors

More attention is being focused on the pattern of drug prescriptions and the hospital staff's attitude on the comparative merits of drugs. Table VI shows various reasons for irrational and costly prescribing.[12]

TABLE VI. Reasons for irrational prescribing

1. Lack of knowledge about drugs
2. Promotional activities by pharmaceutical companies
3. Desire for prestige
4. Too many patients
5. Uncertain diagnosis
6. Therapeutic apprehension
7. Reliance on limited but favourable experience with a drug regardless of scientific evidence

Analyses of prescribing patterns in hospitals and by general practitioners indicate that the main cause of over-prescribing is the pressure put on the doctor to do 'something positive' for the patient. The second factor is the apprehension of missing an underlying disease. The third reason is that the patient expects medication as some kind of a 'social right'.[18]

Attempts have been made by various researchers to suggest improvement in the prescribing habits of clinicians.

It has been observed that even a gentle enquiry like merely asking the prescriber to justify his prescription would result in reducing the consumption of potentially toxic or expensive antibiotics. Although prescribers have insufficient knowledge about drugs, mere dissemination of information has proved to be of little value. Further, it has been shown that effective education in prescribing requires the intervention of a physician as a counselling agent.[19]

Use, Misuse and Abuse of Drugs

There are clear cut examples of underutilization and over-utilization of drugs. For example heparin is most likely underused while Vitamin B_{12}, iron and laxatives are over-used. Some degree of overuse is often combined with partial misuse, e.g. tranquillizers, hypnotics and analgesics.[3]

The medical profession and pharmaceutical industries have been over-enthusiastic in assuring the public that the benzodiazepines are the panacea for every human complaint. These drugs tend to suppress the mental tension that occurs because of social maladjustment, family problems and poor economic conditions.[3]

Many surveys suggest that between 45% and 50% of the antimicrobials used are either inappropriate or given in wrong dosage.[18] It is common knowledge that antibiotics are prescribed irrationally for common cold, surgical prophylaxis and acute gastroenteritis.[18,20]

The micro-organisms isolated between 1917 and 1954 did not carry drug resistant factors with them. Hence, there is a general agreement that antibiotic usage has been responsible for the ecological disturbances in the micro-organisms. The issue is further complicated by the fact that half of the broad spectrum antibiotics produced is added to animal feeds to promote their growth.[21] Hence to counteract resistant organisms we require newer and more potent agents.[22]

Drug Regulations

The patient and health service should be given the earliest possible benefit from improvements in medical science and drug development. Deprivation may result from delays in the introduction of new effective drugs and frustrate enthusiastic professionals and manufacturers. On the other hand the safety of the patient and the efficacy of the treatment must be well documented before a drug is introduced. Serious drug catastrophes such as those which occurred with thalidomide, Clinquinol, practolol and benoxaprofen could have been avoided by such measures.[3] The drug-regulating authorities must control the supply of necessary drugs to the public and ban those which may be toxic or addictive.[12,15,23]

National Drug Policy

There is a need for a national drug policy and its formulation depends on professional skill supported by a strong political will. The objectives of a national drug policy should be to[12]

- provide an adequate quantity of drugs to the population
- eliminate ineffective and inappropriate drugs
- provide administrative and legislative support for ensuring quality and availability of essential drugs
- promote development of local manufacturers where appropriate and necessary
- ensure coordination between the government and the drug supply system
- develop a drug distribution network
- develop a monitoring and information system to prevent wasteful misuse of drugs
- ensure good manufacturing practices
- provide scientific development and application of traditional medicine where appropriate
- develop local manpower for adequate implementation of this drug policy.

Drug Utilization Studies in India

In 1977, a drug utilization study of antimicrobial agents was conducted in JIPMER hospital, Pondicherry. Adopting Kunin's criteria[24] this study found that 67% of in-patients received antimicrobial therapy appropriately. Uppal *et al.*[25,26] have studied drug utilization in the specialities of internal medicine and cardiology at the PGIMER hospital, Chandigarh. Gaitonde[27] has stated that artificially created drug demands by manufacturers lead to the production of non-essential drugs. Based on the findings of a sample survey, Jaju[13] has given suggestions for the practical implementation of supply, storage, distribution, cost and use of drugs by AD 2000—to achieve 'health for all'.

However, insufficient data exist on the drug utilization pattern in primary health centres and comparison of data between different states is lacking. Unlike other countries there is no information on the use of drugs at the national level. Hence many decisions about drugs are taken arbitrarily and their consequences are rarely known.[7]

Recently there has been an increased awareness of cost effective therapy, the essential drug concept and irrational drug combinations.[28] The Clinical Pharmacology Unit of JIPMER, Pondicherry, has taken the responsibility of training interns in these spheres and has also framed a curriculum.[29] India's participation in a pioneering programme at the Karolinska Institute at Stockholm in May and June, 1987 is expected to promote studies aimed at adverse drug reaction monitoring, the social determination of health care, the impact of drug information on a physician's prescribing habits, drug utilization in hospitals, households and villages and patient compliance.[30]

CONCLUSIONS

The use of drugs has become an indicator of health and disease. Accordingly a number of approaches are necessary to identify and analyse the problems related to the causes and consequences of drug utilization. The complexity of the problems needs to be solved urgently by patients, prescribers, politicians and the public.

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