

Review Article

Drug utilization in clinical conditions: an update on its essentials

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ABSTRACT

Drug utilization studies may be defined as studies of the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences. Drug utilization studies can provide highly valuable information, at a reasonable price, on the costs and effects (harmful and beneficial) of drugs. Such studies make available much useful information including indirect data on morbidity, the pharmaceutical component of the treatment cost of an illness, therapeutic compliance, the incidence of adverse reactions, the effectiveness of drug consumption and the choice of comparators. This information can be of great use in the subsequent elaboration of pharmacoeconomy studies, or in the selection of problematic areas in which these studies may be applied. Pharmacoeconomy studies, in turn, can be used to discover the economic repercussions of inappropriate prescribing and to quantify the cost effectiveness of various therapeutic interventions.

The use of drug utilization studies in conjunction with pharmacoeconomic analysis can result in more cost effective utilization of medicines and a better utilization of pharmacoeconomy methods, both of which contribute to a more rational use of drugs.

Keywords: Drug utilization, Pharmacoeconomy, Pharmacoepidemiology

INTRODUCTION

Several studies have been documented that multidrug prescription misuse of drugs, use of unnecessary expensive drugs, poor use of antibiotics and injections which add to the common problem of irrational drug use by prescriber as well consumers.

Rational drug therapy would improve the economics in the management of clinical condition and would prove beneficial to public health. The article reviews the importance of the drug utilization pattern and its essentiality.

History of Drug Utilization Research

Development of drug utilization research dated back to mid 1960's. The initiatives for drug utilization research was taken by United Kingdom and North Europe.^{1,2} Pioneers in this field are Arthur Engel in Sweden and Pieter Siderius in Holland.³ They instilled many investigators with the importance of drug utilization research and the importance of comparing drug use between two different countries and regions. Their work was remarkable, that demonstrated a difference in the sales of antibiotics in six of the European countries. This forced for the world's first meet on drug utilization research in 1969⁴ and led to the constitution of the WHO European Drug Utilization Research Group (DURG) formation.

Pioneers made it clear that investigation should be at the patient level to obtain answers for the following questions such as: why drugs are prescribed, who the prescribers are, for whom the prescribers prescribe, whether patients take their medicines correctly & what are the benefits and risks of the drugs. These were to be obtained with a goal to assess whether the drug therapy is rational or not.

In order to compare the drug utilization in details, a new unit of measurement was introduced that was initially called as agreed daily dose⁵ and later was termed as Defined Daily Dose (DDD).⁶

Defined daily dose (DDD) is a unit that is defined as “the average maintenance dose of the drug when used on its major indication in adults”. The first country to adopt DDD methodology was Czechoslovakia⁷ and the first comprehensive national list of DDDs was published in Norway in 1975.⁸ The first study, making use of DDD method was used to study the anti-diabetic drugs.

Drug utilization research developed quickly and became a subject for consideration at international congresses in pharmacology, pharmacy and pharmacoepidemiology. Rapid developments in the field were particularly noticed in Australia and Latin America.^{9,10} However, it is learnt with the history that a successful research in drug utilization requires multidisciplinary collaboration between clinician, clinical pharmacologist, pharmacist and epidemiologist.

WHAT IS DRUG UTILIZATION RESEARCH AND WHY IT IS NEEDED FOR?

Drug utilization is an important component of many research initiatives that examine the clinical and economic effectiveness of pharmacotherapy. Monitoring the medications use and knowledge of prescription habits are some of the strategies recommended for containing and controlling medication cost and its effect on national budget. So, application of drug utilization monitoring likewise provides further input into utilization correlation with medication effectiveness, prescribing habits, and time dependence.¹¹

DEFINITIONS AND DOMAINS

Definition: Drug utilization research was defined by world health organization (WHO) in 1977 as “the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences”.

Since then, a number of other terms have come into use and it is important to understand the interrelationships of the different domains.

Epidemiology: has been defined as “the study of the distribution and determinants of health related states and

events in the population, and the application of this study to control of health problems”.

Pharmacoepidemiology: includes epidemiological methods applied to studies of the clinical use of drugs in populations. A modern definition of pharmacoepidemiology is “the study of the use and effects/side-effects of drugs in large numbers of people with the purpose of supporting the rational and cost-effective use of drugs in the population thereby improving health outcomes”.

Pharmacosurveillance and pharmacovigilance: are terms used to refer to the monitoring of drug safety, for example, by means of spontaneous adverse-effect reporting systems, case control and cohort studies.¹²

Drug utilization research may be divided into descriptive and analytical studies. Descriptive drug utilization describes the pattern of drug utilization and to identify problems, where as analytical studies link data on drug utilization to figures on morbidity, outcome of treatment and quality of care with the ultimate goal of assessing whether drug therapy is rational or not.

Drug utilization research is an essential part of pharmacoepidemiology. It describes the extent, nature and determinants of drug exposure. Drug utilization studies often employ various sources of information that focus on drugs where pharmacoepidemiology implies defined populations in which drug use can be expressed in terms of incidence and prevalence. However, together they provide insights into the several aspects of drug use and drug prescribing, which include; pattern of use, quality of use, determinants of use and outcome of use.

WHY DRUG UTILIZATION RESEARCH IS NEEDED?

The drug utilization research is aimed to facilitate the rational use of drugs in populations. The research contributes to rational drug use in the following ways;

Description of drug use pattern

It can be used to estimate the numbers of patients exposed to specified drugs within a given time period. Such estimates may either refer to prevalence and incidence. Extent of use at a certain moment and/or in a certain area can be described. It can estimate the use of drug, whether properly used, overused or underused, the pattern or profile of drug use.¹³

Such research enables us to compare the observed patterns of drug use with current recommendations and guidelines, and also helps in assessing the quality indicators for patterns of drug utilization.

Signals of irrational use of drugs

The drug utilization research (DUR) can help us avoid prolonged irrational use of drugs. Geographical differences and changes in drug have medical, social and economical implications which should be identified, explained and, when necessary corrected. The observed patterns of drug use can be compared with the current recommendations. Following this, based on the hypothesis generated it can be determined whether the discrepancies are less than optimal practice, need interventions or whether the guidelines should be reviewed in the light of actual practice.^{14,16}

Steps to improve drug use –follow up

This is necessary because the total cost to society may remain the same or may even increase if more expensive drugs are used as alternatives. This can be improved by monitoring and evaluating the provision of regional or local formularies made use, the impact of regulatory changes and the extent to which the pharmaceutical industry affect the pattern of drug use.^{15,16}

Quality control of drug use

In order to ensure continuous quality improvement it is essential to make use of the drugs according to a quality control cycle that can be applied at many level ranging from local or regional discussion among physician, clinical pharmacologist or pharmacist etc.

DRUG UTILIZATION STUDIES

The drug utilization studies that were initially conducted in Estonia and Latin America facilitated to initiate and modify the rational drug policy at both national and local levels.¹⁶

Information of drug use

The different types of drug use information such as; drug groups, over all use of drugs, individually generic compounds or specific products are very important in the drug utilization research. The types of drug information include¹⁷;

Drug based information

The trend in drug use includes aggregation of data on drug use at various levels, information on indication, doses and dosage regimen are essential to answer several clinically important questions.

For drug with multiple indications it is important to divide data according to indication to allow correct interpretation. For example, one has to analyze the situation in which the antibiotic is indicated or not, to know if the condition for which it is used is rational or not.

Importance has to be given to the dose administered. Drugs can be administered based on the prescribed daily dose (PDD) which means an average dose as obtained from a representative sample of prescriptions. PDD will differ for different indication of the same drug, so it is essential to interpret the overall use data.^{18,19}

Problem based information

It is important to address the question as to how a particular problem e.g. sore throat, hypertension or gastric ulcer would be managed. To obtain this it is important to gather information such as drug treatment v/s non drug treatment, severity of problem, new or continuous problem, duration of treatment, medication used, how the medications were supplied and other medications prescribed etc.¹⁶

Patient information

Information on the demographic factor such as age, gender, ethnicity, co-morbidities, knowledge, belief and perception etc are important to be considered in DUR, for e.g., age distribution is of critical importance, to assess the likelihood of severe adverse effects with non-steroidal anti-inflammatory drugs (NSAIDs). Another few examples that can be mentioned are, in the management of hypertension, beta blockers should not be used to treat patient with asthma, and similarly ACE inhibitors are preferred in patient of heart failure etc.

Prescriber's information

Prescriber plays a very important role in determining the drug use. Various factors such as age, gender, medical school, years in practice, type of practice (specialist/family, rural or urban), practice size, patient mix, knowledge about drugs, etc influence the drug use.^{16,17} As use of drug also depends on the prescriber choice ('p' drug).

Drug cost

Data on drug costs is important in managing the policies related to drug supply, pricing and their use. One has to consider affordability and accessibility for the drug used. Costs may be determined at various levels such as government, health facility, hospital, health maintenance etc.^{17,18}

SOURCES OF DATA ON DRUG UTILIZATION

The drug-use chain includes processes to obtain their storage, distribution, prescribing, patient compliance and the review on outcome of treatment at various levels in the health care system. Source of drug utilization data varies from country to country and depends upon the level of record keeping, data collection, analysis, reporting and the operational considerations of the health care system.

Data can be obtained by large database, from the drug regulatory agencies, suppliers etc, such data obtained is used to describe quantities of specific drugs, drug group, supplier and type.

Practice setting data

Data from various health facilities may be used to evaluate specific aspects of health provision and drug use, information on prescribing habits and other aspects related to patient care. These include the prescribing data, dispensing data, drug use indicators etc.¹⁹

Community setting data

Often the drugs available in households have either been prescribed or dispensed at health facilities, purchased at a pharmacy or are over-the-counter medications. The drugs may be for the treatment of a current illness or are left over from a previous illness. This is best assessed by performing household surveys, counting leftover pills and by reviewing treatment sheets.²⁰

Drug use evaluation

Evaluation of drug use in treating any condition is referred to as drug utilization review which is a continuous, systematic, criteria-based drug evaluation that ensures the appropriate use of drugs.²¹

By drug utilization review it is possible to obtain the information regarding problems related to drug use, means to correct the problem which helps in rational drug therapy. The drug use evaluation may be based on data collection prospectively or retrospectively.

ECONOMIC ASPECT OF DRUG USE (PHARMACOECONOMY)

Cost of the drugs used in the treatment of any condition is important because ultimately it reflects the cost of health care in both developed and developing countries. Sometimes money spent on one drug may happen to save cost in other areas.²² For example, the purchase of one specific type of drug may lead to reductions in the following; use of other drugs, the number of patients requiring hospitalization or in the length of stay, the number of doctor visits required administration and laboratory costs.

Cost may arise from adverse drug reactions both in case of short term and long term use of drugs in treatment requiring extra health benefit that can be achieved to weigh against extra net cost.

Concern regarding the cost of medical care in general and pharmaceuticals are expressed by all health system.²³ However, there is a general focus on providing quality care within limited financial resources. Some of the concepts used to decide for policy formulation and

implementation include; cost minimization, cost effectiveness, cost benefit and cost utility.

Cost minimization analysis

It is a method of calculating drug costs in order to project the least costly drug or therapeutic modality. It also reflects the cost of preparing and administering a dose. It is often used in evaluating cost of a specific drug. It helps in comparing two products that have been shown to be equivalent in the dose and therapeutic effect.²⁴ Hence, the method is useful for comparing generic and therapeutic equivalent drugs or me too drugs.

Similarly, if new therapy were not safer or effective than an existing therapy, it would justify same price as the existing therapy.²⁵ For e.g.; introduction of new ACE inhibitors with essentially same properties as existing members of the class, then the price would be equivalent to that of the existing drug.

Cost effectiveness analysis

It is a comprehensive analysis while cost of the drug is measured in monetary terms, the effectiveness of the drug is determined independently, measured in terms of clinical outcome such as numbers of lives saved, complications prevented or diseases cured.²⁶

It measures the increment cost of achieving health benefit and is expressed on particular health outcome that varies according to indication for the drug. However, it is difficult to make judgment about the value of money across a range of drug group and health outcomes.

Cost utility analysis

This is a process that is used to determine cost in terms of utilities, especially quantity and quality. Unlike cost-benefit analysis, cost-utility analysis is used to compare two different drugs or procedures whose benefits may be different.^{26,27} It expresses the value for money in terms of a single type of health outcome. This approach incorporates both increases in survival and changes in quality of life as one measure. This also allows an easy comparison across different types of health outcome and provides broader context which enables to judge the value for money of using a particular drug.

Cost benefits analysis

The cost benefit analysis is used to value both the incremental cost and outcomes in monetary terms and therefore allows calculation of the net monetary cost of achieving a health outcome.^{28,29}

DRUG CLASSIFICATION SYSTEM

The system is for describing the drug assortment in a country or region and is a prerequisite for national and

international comparisons of drug utilization data, which have to be collected and aggregated in a uniform way.

The purpose of having an international standard is that it enables us to compare data between the countries. Drugs can be classified according to their chemical structure. Drugs may be used for two or more equally important indication, and the main therapeutic use of a drug may differ from one country to another. This would often results in possible alternatives for classification. However, national traditions have to be weighed against the opportunity for comparison of drug utilization.

One such classification is Anatomical Therapeutic Chemical Classification (ATC) that includes classification of drugs into different groups according to the organ or system on which they act and according to their chemical, pharmacological and therapeutic properties.³⁰

Implementation of ATC/DDD methodology

The linkage between the national drug register and ATC/DDD has to be ascertained by the persons with proper knowledge of the methodology. There are guidelines available for ATC classification and DDD assignment that give information for allocating ATC codes and DDDs at national or local level.^{30,31} All efficacy assigned ATC codes and DDDs are listed in the ATC index with DDDs, update every year.

DRUG UTILIZATION METRIC AND THEIR APPLICATION

The defined daily dose is the assumed average maintenance dose per day for a drug used for its main indication in adults. It is a unit of measurement and does not necessarily correspond to the recommended or prescribed daily dose [PDD]. Doses for individual patient and groups will often form DDD as they must be based on individual characteristics and pharmacokinetics consideration.³²

Prescribed daily dose and consumed daily dose

The prescribed daily dose (PDD) is defined as the average dose prescribed according to a representative sample of prescriptions. It can be determined from studies of prescriptions or medical or pharmacy records. It will give the average daily amount of a drug that is actually prescribed. It is important to consider discrepancy between the PDD and the defined daily dose (DDD) while evaluating and interpreting drug utilization figures.³³

In case of some drugs where the recommended dosage differs from one indication to another, it is important to link the diagnosis to the PDD. Pharmacoepidemiological information is very important to interpret a PDD. The PDD vary according to the illness treated and therapeutic

traditions of the nation. They also vary between different countries. Therefore it is essential to consider this fact while making an international comparison.

Other units for presentation of volume

Some common physical units such as grams, kilograms and liters, numbers of packages or tablets and numbers of prescriptions are also used for drug utilization research, but have certain disadvantages.^{33,34} For example grams of active ingredient, counting of number of tablet which does not reflect variation in strength of tablet and the number of prescriptions which do not accurately reflect the total use. Therefore these units can be applied only when the single drug or of well-defined product is evaluated.

Cost

Drugs use can be also expressed in term of cost which can be analyzed in the form of drug expenditure. However, international comparison can be misleading and have limited value. Moreover the price differences between alternative preparation and national cost level make it difficult for evaluation.³⁴ Trends in drug use measured in cost may therefore look very different from the same drug use measured in DDDs.

CONCLUSION

Inappropriate and irrational drugs use is wide spread in private sectors and at community level which are often overlooked. More of the research on different types of intervention strategies in various health care settings is essentially needed to draw conclusion on effectiveness of specific intervention strategies. All the more research is needed on sociocultural factors influencing the impact of drug use interventions. Many efforts at various levels are essential to be undertaken to improve the drug use, avoid irrational use and adverse drug reactions.

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