Chapter

1

Introduction to Pharmacotherapeutics

The term "Pharmacotherapeutics" consists of two words that is '*Pharmaco*' (*a Latin word*) which means 'drug' and '*Therapeutics*' which concern with 'effective use'.

Therefore, it is a branch of medical pharmacology which principally concern with the safety, therapeutic use and effects of drug administration or pharmacotherapeutics is the branch of medical science that deals with interventions related to administration of drugs (pharmacokinetics) and their mechanism, effects, interactions and side effects (pharmacodynamics) as shown in Fig. 1.1.

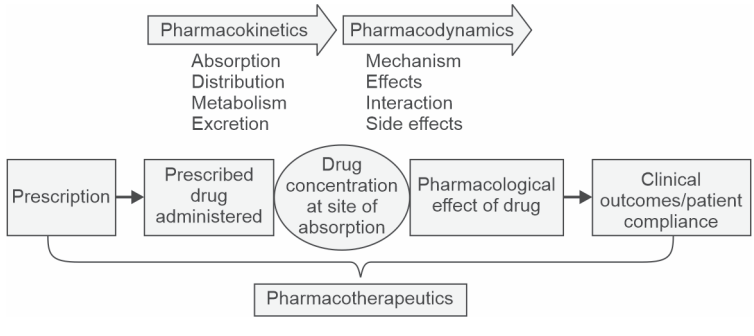

Fig. 1.1: Diagrammatic illustration of pharmacotherapeutics

Objectives

Various objectives of pharmacotherapeutics are as follows:

i. Understanding the therapeutic applications of drugs, based on their underlying pharmacokinetics and pharmacodynamics.

ii. Ensure the proper and rational use of drugs.
iii. Avoid or reduce adverse drug reaction (ADR) and toxicity.
iv. Provide optimum level quality and effective products at a minimum drug cost.
v. Utilize and explore advance knowledge made by researchers.
vi. Understanding pathophysiology of disease and the rationale for drug therapy.
vii. Therapeutic approach for the management of chronic diseases.
viii. Identify the patient specific parameters relevant in initiating drug therapy and adverse effects.
ix. Understanding drug monographs and exploring their individual clinical indications/contraindications, precautions, MOA (mechanisms of action), side effect profiles, brand names and brand substitution.
x. Appreciate that medicines may produce adverse effects and various interactions with varying severities.
xi. Develop an understanding of the mechanisms underlying adverse reactions, the principles for prevention and therapeutic management.
xii. Understanding the severity of disease, effect of drugs and the genetic makeup of individuals.
xiii. Discuss specific drug interactions and explore recommendations in prevention and treatment.
xiv. Participate in multiple case presentations.
xv. Ensures patient compliances.

RATIONAL USE OF MEDICINES

The rational use of medicines was firstly introduced by WHO in 1985 in a conference of experts held in Nairobi, Kenya.

As indicated by WHO, "Rational use of medicines requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost".

Criteria for Rational use of Medicines

Usually rational use of medicines is confirmed by 5 R strategies which includes:

i. **Right drug:** The selection of drugs is based on efficacy, safety, suitability and cost considerations.
ii. **Right dose:** Proper selection and duration of medicines to prevent resistance.
iii. **Right patient:** Preventing use of drug in patients who can be treated with healthy alternatives.
iv. **Right time:** Preventing prescribing error by double check the prescription.
v. **Right route:** Patients should be provided with relevant, accurate, important and clear information regarding his/her condition and the medication that are prescribed.

Steps of Rational use of Medicines

There are seven major steps of rational use of medicines which are as follows:

i. **Step I:** Identify the patient's problem based on symptoms and recognize the need for action.
ii. **Step II:** Diagnosis of the disease—define the diagnosis.
iii. **Step III:** List possible intervention or treatment (drug or no drug)—identify the drug.
iv. **Step IV:** Start the treatment by writing an accurate and complete prescription, e.g. name of drugs with dosage forms, dosage schedule and total duration of the treatment.
v. **Step V:** Give proper information, instruction and warning regarding the treatment, e.g. side effects, ADR and dosage schedule.
vi. **Step VI:** Monitor the treatment to check, if the particular treatment has solved the patient's problem.
vii. **Step VII:** Explain him what to do if the treatment is not effective or if too many side effects occur.

Why Medicines use Irrationally?

There are too many reasons to prescribing medicines irrationally; some of them are described below:

i. **Lack of information:** Unlike many developed countries we do not have regular facility which provides us up to date unbiased information on the currently used drugs. Majority of our practitioners rely on medical representatives. There are differences between pharmaceutical concern and the drug regulatory authorities in the interpretation of the data related to indications and safety of drugs.

ii. **Inadequate training and education of medical graduates**: Lack of proper clinical training regarding writing a prescription during training period, dependency on diagnostic aid, rather than clinical diagnosis, is increasing day by day in doctors.

iii. **Poor communication between health professional and patient:** Medical practitioners and other health professional giving less time to the patient and not explaining some basic information about the use of drugs.

iv. **Lack of diagnostic facilities/uncertainty of diagnosis:** Correct diagnosis is an important step toward rational drug therapy. Doctors posted in remote areas have to face a lot of difficulty in reaching to a precise diagnosis due to nonavailability of diagnostic facilities. This promotes polypharmacy.

v. **Demand from the patient:** To satisfy the patient expectations and demand of quick relief, clinician prescribe drug for every single complaint. Also, there is a belief that "every ill has a pill" All these increase the tendency of polypharmacy.

vi. **Defective drug supply system and ineffective drug regulation:** Absence of well organized drug regulatory authority and presence of large number of drugs in the market leads to irrational use of drugs.

vii. **Promotional activities of pharmaceutical industries:** The lucrative promotional programmes of the various pharmaceutical industries influence the drug prescribing.

Policies to Promote Rational use of Medicines

WHO promotes 12 key interventions to encourage more rational use:

i. Establishment of a multidisciplinary national body to coordinate policies on medicine use.
ii. Use of clinical guidelines.
iii. Development and use of national essential medicines list.
iv. Establishment of drug and therapeutics committees in districts and hospitals.
v. Inclusion of problem-based pharmacotherapy training in undergraduate curricula.
vi. Continuing in-service medical education as a licensure requirement.
vii. Supervision, audit and feedback.
viii. Use of independent information on medicines.
ix. Public education about medicines.
x. Avoidance of perverse financial incentives.
xi. Use of appropriate and enforced regulation.
xii. Sufficient government expenditure to ensure availability of medicines and staff.

EVIDENCE-BASED MEDICINES

The idea of evidence-based medicine (EBM) was firstly proposed by an epidemiologist 'Archie Cochrane' at the Mc Master University in Canada in 1988 but during the 1990s became known throughout the world.

Evidence-based medicine is a set of principles and methods intended to ensure that the greatest extent possible, medical decisions, guidelines and other types of policies are based on consistent with good evidence of effectiveness and benefit.

Aim

EBM aims that healthcare professionals should make conscientious, explicit and judicious use of current best evidence in their everyday practice.

Objectives

The objectives of EBM are to improve the quality of care through the integration of best available evidence from the clinical research, some of which are:

i. To recognize information needed while caring a patient.
ii. To identify the best existing evidence to help or resolve the problems.
iii. To integrate the evidence into a medical plan.

Importance of EBM

EBM is being changed a way, in which patient treated by:

i. Improving quality of care through the identification and promotion of practices.
ii. Promoting critical thinking.
iii. Effectiveness of clinical interventions.
iv. Accuracy and precision of diagnostic tests.
v. Elimination of ineffectiveness or harmfulness.

Five 'A's Strategies of EBM (Fig. 1.2)

i. Step I—Ask (Formulate Clinical Questions)

While practicing EBM, it is one of the difficult steps to translate the clinical problem into an answerable question. Patient comes with a problem and various questions for which practitioner would like to answer. These questions are usually unstructured and complicated and sometime may not be clear in mind.

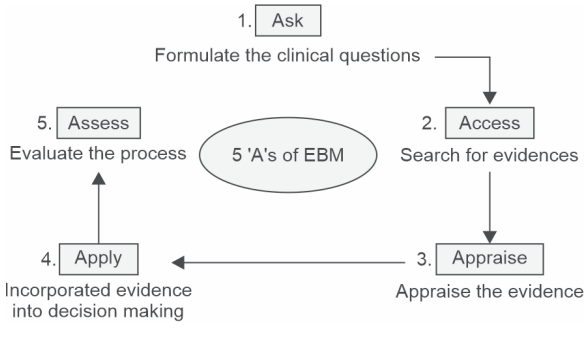

Fig. 1.2: Effective EBM method

Therefore, practicing of EBM should begin with a well-formulated clinical question. Good clinical questions should be a clear, problem-oriented and answerable after searching medical literature. Good clinical question should be structured in the **PICO** (**P**atient or **P**roblem, **I**ntervention, **C**omparison, **O**utcome/s) or **PIO** (**P**atient or **P**roblem, **I**ntervention, **O**utcome/s) format.

PICO format

i. The patient or problem—who is the relevant patients and what kind of problem we try to solve?
ii. The intervention—what is the management strategy, diagnostic test or exposure (drugs, diagnostic test, foods or surgical procedure)?
iii. Comparison of interventions—what is the control or alternative management strategy, test or exposure that we will compare?
iv. The outcome—what are the patient-relevant consequences of the exposure in which we are interested?

Types of clinical questions to be asked

a. Questions about intervention
b. Questions about etiology and risk factors
c. Questions about frequency and rate
d. Questions about diagnosis
e. Questions about prognosis and prediction
f. Questions about cost-effectiveness
g. Questions about phenomena

ii. Step II—Access (Search for Evidences)

After formulating the clinical questions, the next step is to seek relevant evidence that will help you to answer the questions. There are several sources of information that may be of help. Traditional sources of information such as textbooks and journals are often too disorganized or outdated. You may ask to experts but the quality of information obtained from this source is variable. Secondary sources of reliable evidence which

may help provide quick evidence-based answers to specific clinical questions include:

a. Archimedes (http://adc.bmjjournals.com/cgi/collection/archimedes).
b. Clinical evidence (http://www.clinicalevidence.com/ceweb/conditions/index.jsp).
c. BestBets (http://www.bestbets.org/index.html).
d. Health Technology Assessment (HTA) database

iii. Step III—Appraise (Appraise the Evidence)

After collecting all the relevant evidences on a subject, the next step is to appraise the evidence for its validity and clinical usefulness. Appraising provide a structured but simple method for assessing research evidences in three major areas including validity, importance and applicability to patients. Therefore, several tools for appraising research articles are available; these include tools for appraising randomized controlled trials, systematic reviews, case–control studies and cohort studies. These tools are simple, easy to use and freely available on the internet.

Note: Putting unreliable evidence into practice could lead to harm.

iv. Step IV—Apply (Incorporated Evidence into Decision Making)

After critical appraisal, we decided that a piece of evidence is valid and important then also decide whether that evidence can be applied patient. In deciding this, the evidence regarding both efficacy and risks should be fully discussed with the patient or parents or both, in order to allow them to make an informed decision. This approach allows a 'therapeutic alliance' to be formed with the patient and the parents and is consistent with the fundamental principle of EBM.

The questions that we should ask before the decision to apply the results of the study are:

a. Are the participants in the study similar enough to my patient?

b. Is the treatment available and is healthcare system prepared to fund it?
c. What alternatives are available?
d. Do the potential side effects of the drug or procedure outweigh the benefits?
e. Are the outcomes appropriate to the patient? Does the treatment conflict with the patient's values and expectations?

v. Step V—Assess (Evaluate the Process)

As we incorporate EBM into routine clinical practice, we need to evaluate our approach at frequent intervals and to decide whether we need to improve on any of the four steps discussed above.

The EBM-oriented clinicians have three tasks

a. To use evidence summaries in clinical practice.
b. To help develop and update selected systematic reviews or evidence-based guidelines in their area of expertise.
c. To enroll patients in studies of treatment, diagnosis and prognosis on which medical practice is based.

ESSENTIAL MEDICINES LIST

The first list of essential medicines was released in 1977 by WHO which contain 186 drugs and the first essential medicines list for children was published in 2007.

As per WHO "Essential medicine list (EML) is a collocation of essential medicines that satisfy the healthcare needs of population at all time". They are selected on the basis of disease prevalence and public health relevance, evidence of efficacy and safety and comparative cost-effectiveness.

The WHO model lists of essential medicines are updated every two years by the Expert Committee on selection and use of essential medicines. The current versions, updated in September 2021, are the 22nd essential medicines list (EML) and the 8th essential medicines list for children (EMLc).

Inclusion Criteria of Medicines in EML

i. The medicine should be approved and should be cost-effective.
ii. It should have a proven efficacy and safety profile based on valid scientific evidence.
iii. It should be useful in disease which is a public health problem.
iv. The medicine should be aligned with the current treatment guidelines for the disease.
v. It should be stable under the storage conditions.

Exclusion Criteria of Medicines in EML

i. Medicine has been banned by country.
ii. There are reports of concerns about the safety profile of a medicine.
iii. A medicine with better efficacy or favorable safety profiles and better cost-effectiveness is available.
iv. The disease burden for which a medicine is indicated is no longer a national health concern.
v. In the case of antimicrobials, if the resistance pattern has rendered a medicine ineffective in the country context.

Process of New Medicine to get in EML

There are total seven steps to get a new medicine on the WHO model list of essential drugs:

i. Identification of public health need for a medicine.
ii. Development of the medicine; phase I–III trials.
iii. Regulatory approval in a number of countries.
iv. More experience under different field circumstances; post-marketing surveillance.
v. Price indication for public sector use.
vi. Review by WHO disease programme; define comparative effectiveness and safety in real-life situations, comparative cost effectiveness and public health relevance.
vii. Submission to WHO Expert Committee on essential drugs.

Components of 22nd List of Essential Medicines

1. **Anesthetics:**
   - 1.1 General anesthetics and oxygen
   - 1.2 Local anesthetics
   - 1.3 Preoperative medication and sedation for short-term procedures
2. **Medicines for pain and palliative care:**
   - 2.1 Nonopioids and nonsteroidal anti-inflammatory drugs (NSAIDs)
   - 2.2 Opioid analgesics
   - 2.3 Medicines for other common symptoms in palliative care
3. **Antiallergics and medicines used in anaphylaxis.**
4. **Antidotes and other substances used in poisonings:**
   - 4.1 Nonspecific
   - 4.2 Specific
5. **Anticonvulsants/antiepileptics.**
6. **Anti-infective medicines:**
   - 6.1 Antihelminthics
   - 6.2 Antibacterial
   - 6.3 Antifungal medicines
   - 6.4 Antiprotozoal medicines
7. **Antimigraine medicines:**
   - 7.1 For treatment of acute attack
   - 7.2 For prophylaxis

Note: To see the full list of essential medicines kindly visit https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.03 site.

Importance of EML

The implementation of concept of essential medicines has logistic and prescribing importance:

i. Better medicines management that is easier procurement, storage and distribution.
ii. More manageable stock.
iii. Better quality assurance.

iv. Less prescription error due to proper training and drug information.
v. Better recognition of adverse drug reactions.

STANDARD TREATMENT GUIDELINES

Standard treatment guidelines (STGs) also termed clinical guidelines and clinical protocols, are the component of health-care services which play a critical role in ensuring evidence-based clinical practice and quality of care. It includes:

i. The list of preferred pharmacological and nonpharmacological treatment for common health problems experienced by people in a specific health system. The pharmacological treatment should include the name, dosage form, strength, average dose (pediatric and adult), number of doses per day and duration of treatment.
ii. Other information on diagnosis and advice to the patient may also be included. The most common diseases and serious medical conditions that have high morbidity and mortality rate are selected.
iii. Treatment guidelines must have the most up-to-date and evidence-based information to determine appropriate treatment options by expert authors and reviewers.
iv. Clinical condition.
v. Diagnostic criteria and exclusions.
vi. Treatment objectives (e.g. elimination of Plasmodium parasites from a blood smear).
vii. Referral criteria.
viii. Patient education information.
ix. What to do when clinical response is poor?

Process of STGs Development

Ministry of Health and Family Welfare commissioned a Task Force on standard treatment guidelines, which comprised of eminent clinicians and representations from important stakeholders such as ICMR, DGHS, FICCI, civil society

organizations and academic institutions which develops, review and updated the STGs.

There are ten steps of development of STGs as shown in Fig. 1.3.

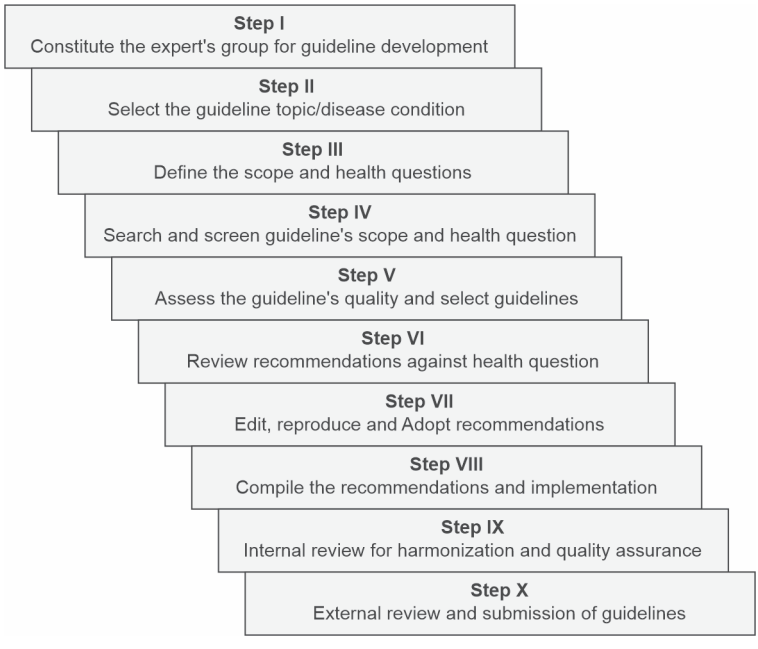

Fig. 1.3: Process of STGs

Advantages of STGs

STGs are beneficial to healthcare providers, healthcare officials, supply management personnel and patients in the following ways:

i. **For healthcare providers:**
   a. Provides standardized guidance to practitioners.
   b. Encourages high quality care for specific conditions by directing to practitioners.
   c. Encourages the best quality of care since patients are receiving optimal therapy.

d. Utilizes only formulary or essential medicines, so the healthcare system needs to provide only the medicines in the STGs.
e. Provides valuable assistance to all practitioners, especially to those with lower level skills.
f. Enabled providers to concentrate on making the correct diagnosis because treatment options will be provided for them.

ii. **For health care officials:**
a. Provides a basis for evaluating quality of care provided by the healthcare professionals.
b. Provides the most effective therapy.
c. Provides a system for controlling cost by using funds.
d. Provides information for practitioners to give to patients concerning the institution's standards of care.

iii. **For supply management:**
a. Utilizes only formulary or essential medicines
b. Provides information for forecasting and provides information for purchase of prepackaged medicines

iv. **For patients:**
a. Patients receive optimal pharmaceutical therapy
b. Enables consistent and predictable treatment from all levels
c. Allows for improved availability of medicines
d. Helps to provide improved outcomes because patients are receiving the best treatment regimens available
e. Lowers cost

ISOLATED KEY POINTS

- The term "Pharmacotherapeutics" consists of two words that is '*Pharmaco*' (*a Latin word*) which means 'drug' and '*Therapeutics*' which concern with 'effective use'.
- Pharmacotherapeutics is a branch of medical pharmacology which principally concern with the safety, therapeutic use and effects of drug administration.

- Rational use of medicines requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost.
- Criteria for rational use of medicines are:
  i. Right drug
  ii. Right dose
  iii. Right patient
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- EBM: Evidence-based medicine is a set of principles and methods intended to ensure that the greatest extent possible, medical decisions, guidelines and other types of policies are based on consistent with good evidence of effectiveness and benefit.
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