(18)

GOVERNMENT OF JAMMU & KASHMIR
SHER-I-KASHMIR INSTITUTE OF MEDICAL SCIENCES
SOURA SRINAGAR

Syllabus for Assistant Professor Posts of the Department of Clinical Pharmacology,

SKIMS, SOURA.

A. General pharmacology

- History of development, definition and scope of clinical pharmacology
- Basic pharmacokinetic (PK) principles - ADME (Absorption, Distribution, Metabolism and Excretion) of drugs, membrane transporters
- Studies on bioavailability of drugs including novel dosage forms, drug-drug and drug food interactions, enzyme induction and inhibition,
- Therapeutic drug monitoring – drugs requiring Therapeutic drug monitoring (TDM), dosage adjustments based on physiological or pathological changes, dose optimization strategies
- Population pharmacokinetics: sources and correlates of variability in drug concentrations in patients
- Dose response relationship, PK-PD modelling and simulation
- Physiologically-based pharmacokinetic (PBPK) modeling and simulation - the effects of extrinsic factors viz. concomitant drugs, food and intrinsic factors viz. age, organ dysfunction, disease status, and genetics on drug exposures
- Basic pharmacodynamic (PD) principles – molecular basis of drug action
- Drug disease, drug host, drug environment interactions - mechanisms and clinical importance
- Drug use in special prescribing situations – in children, elderly, during pregnancy, lactation, organ dysfunction – hepatic, renal, cardiac etc., malnutrition
- Pharmacogenomics – application of pharmacogenomics in therapeutic decision making and optimization of clinical care, precision/ personalized medicine, major alleles and frequencies in African and European population, gene based dosing recommendation for selected drugs, classification of G6PD deficiency (WHO-working group), genetic variations in transporters, drug induced hypersensitivity reactions, epi-genomics.
- Animal toxicology and PK-PD data relevant to clinical evaluation of new drugs
- Nomenclature of drugs
- Pharmaco-epidemiology - basic principles of epidemiology, study designs, confounding and bias, analysis and interpretation of data, survival analysis, propensity score methods
- Pharmaco-economics-fundamental concepts and methods, terminology, role in drug development and healthcare decision making and formulary management.

B. Systemic pharmacology

- Cardiovascular system - ischemic heart disease, hypertension, heart failure, circulatory shock, cardiac arrhythmias, stroke, hyperlipidemias and pulmonary arterial hypertension and metabolic syndrome
- Central nervous system - epilepsy, psychosis, depression, mania, anxiety, sleep disorders, general and local anesthetics, opioid analgesics, neurodegenerative disorders, drug addiction.
- Pulmonary pharmacology (common bronchopulmonary diseases. like bronchial asthma, COPD, pulmonary fibrosis and pulmonary function tests)
- Genitourinary system - kidney diseases, acute kidney injury, chronic kidney disease, renal failure, urolithiasis, benign prostatic hypertrophy and prostatic carcinoma
- Gastrointestinal pharmacology – peptic ulcer, GERD, GI motility disorders, inflammatory bowel disease, irritable bowel syndrome.
- Hepatobiliary systems, viral hepatitis, nonalcoholic fatty liver disease, cirrhosis
- Hormones and hormone antagonists – thyroid, female reproductive system, male reproductive system, adrenals, pancreas including diabetes mellitus, bone mineral homeostasis, hypothalamic pituitary axis.
- Cytotoxic and targeted cancer chemotherapy, hormones and related agents in cancer therapy.
- Immuno-pharmacology- immune-suppressants – glucocorticoids, calcineurin inhibitors, antiproliferative and antimetabolic agents, biologics, immunological reactions to drugs and drug allergy.

- Ocular pharmacology – drug delivery strategies, ophthalmic uses of drugs - antimicrobials, autonomic agents, anti-inflammatory, immunomodulatory agents, drugs for retinal neovascularization and macular degeneration, ocular adverse effects of drugs.
- Dermatologic pharmacology
- Pharmacotherapy of inflammation, pain, fever
- Chemotherapy of infectious diseases- bacterial, viral, fungal, protozoal, helminthic and other infections
- Nutraceuticals
- Clinical pharmacology of drugs used in cardiovascular, CNS, renal, pulmonary, gastrointestinal tract, infective, and other disorders
- Common malignant diseases- pathophysiology, drug targets
- Drugs for neglected diseases initiatives in India

C. Use of drugs for diagnostic purposes

- Special contrast media
- Radionuclide imaging
- Imaging in drug development

D. Research methodology and medical biostatistics

- Sampling methods, design for observational studies,
- Interventional and epidemiologic study designs, confidence interval, principles of test of significance, sample size, type I and type II error,
- Qualitative research methods ,
- Data types and choice of statistical methods
- Descriptive statistics measures and graphs
- Sample size determination and power analysis
- Statistical test, Parametric and non-parametric tests
- Tests for comparing proportions
- Correlation and regression
- Statistics of diagnostic tests
- Logistic regression, multiple regression
- Survival analysis
- Critical interpretation of statistical outputs including P-values and confidence intervals, multiple hypothesis testing
- Principles of interim analysis of clinical trial data
- Overview of statistical software
- Basics of data management
- Role of biostatistician in protocol designing
- Principles of critical appraisal of literature, levels of evidence and quality of evidence
- Role and limitations of evidence in development of guidelines.

E. Clinical trials, BA/BE studies, Bioequivalence and allied topics

- Salient features of various phases of clinical trials, principles of controlled clinical trials, sequential trials, crossover trials, adaptive trials and registries
- Special considerations for Phase I studies – principles of First in Human (FIH) dose determination, pharmacokinetic studies, human pharmacodynamic studies, tolerance, single dose/ multiple dose, dose escalation, infrastructure requirements
- Phase II: Dose selection, study designs, selection of subjects, proof of concept studies, dose ranging studies
- Phase III: Study designs, multicenter trials, global trials, site selection
- Post-marketing studies: types of studies and their objectives, post-marketing surveillance, phase IV trials, Periodic safety update/assessment reports
- Principles and methods of Bioequivalence studies

- Multicentric studies: organization, standardization, quality control, training, protocol compliance, data processing, central randomization, issues
- Use of placebo: pharmacology of placebo, historical aspects, active/inert placebo, placebo reactors, ethics of placebo.
- Washouts and run-in periods: needs, ethics, duration
- Withdrawals, dropouts, and missing values: problems, handling of data
- Clinical trial designs including herbal medicines and AYUSH medicines – history, present status, standardization, preclinical evaluation, special issues and their solutions, regulatory aspects.
- Protocol design, Case Report Form (CRF), design of standard operating procedure (SOP) development
- Adaptive designs of clinical trials, platform trials, basket trials, umbrella designs
- Interim analysis
- Randomization, blinding and other bias control measures – need, methods, issues and their solutions
- Endpoints and biomarkers (including surrogates) – selection in specific therapeutic areas.
- Stopping rules
- Superiority, inferiority, and equivalence trials
- Per-protocol and intention-to-treat analysis
- Role of monitors, inspectors, auditors, Data Safety Monitoring Board (DSMB)
- Special considerations for bioequivalence and bioavailability (BA/BE) studies.
- Specific topics: academic trials, collaborative research, compensation for participation and trial related injury, trial insurance, compliance monitoring, quality of life assessment.
- Clinical and preclinical development of vaccines
- Clinical trials of repurposed drugs.

F. Ethics in clinical practice and research, including

- Historical evolution of principles of ethics
- Principles of risk benefit assessment
- Nuremberg code, Belmont report, Declaration of Helsinki
- Indian Council of Medical Research (ICMR) ethics guidelines, ethics of pediatric research, pandemic research, research integrity and publication ethics
- Ethical dilemmas in clinical practice and research
- Role of the ethics committee, informed consent
- Vulnerable subjects in clinical research
- Ethics of clinical practice, for e.g., resource allocation in pandemics, organ transplant, euthanasia
- Audiovisual consent.

G. Preclinical studies and their assessment

- Animal pharmacology – efficacy and safety studies, assessment of adequacy of data
- Pharmacokinetics and toxicokinetic studies
- Toxicity studies: acute, subacute, chronic
- Mutagenicity, carcinogenicity, reproductive toxicity, special toxicity studies, safety pharmacology studies, QT prolongation studies
- Good laboratory practices, OECD principles.

H. Pharmaceutics and drug discovery

- Drug formulations, pharmaceutical equivalence
- Good manufacturing practices
- Bioavailability, bioequivalence and bioequivalence studies
- New drug delivery systems
- Screening of chemical compounds, high throughput screening
- Computer assisted drug designing

- General pharmacology and systematic screening.
- Techniques in drug discovery: bioinformatics, proteomics and metabolomics.
- Role of FDA in drug development
- Role of imaging in drug development-molecular imaging techniques and imaging therapeutic drug effects

I. Rational use of medicines, including:

- Principles of rational use of medicines
- Essential medicine lists
- Drug Formularies
- Standard treatment guidelines or protocols from Indian Council of Medical Research, Ministry of Health and Family Welfare and other professional bodies
- Rationality of fixed dose combinations
- Antibiotic policy and antimicrobial stewardship programs for respective medical institutions – role of a clinical pharmacologist – principles, methods, prospective audit and feedback, formulary restriction, educational interventions, guidelines, IV oral switching, dose optimization, timeouts, antibiotic use measures, special situations viz. intensive care, healthcare acquired infections, immuno-compromised patients etc.

J. Regulatory affairs, including

- Good Clinical Practice – role and responsibilities of stakeholders
- Good Laboratory Practice, Good Clinical Laboratory Practice and Good Manufacturing Practice, Other quality guidelines/ regulations – GxP (a collection of quality guidelines and regulations created to ensure that bio/pharmaceutical products are safe, meet their intended use, and adhere to quality processes during manufacturing, control, storage, and distribution)
- Drug laws applicable in India, new drug clinical trial Rules, 2019
- Structure and functions of drug control authority (Central Drugs Standard Control Organization), State Licensing Authorities
- Drug price control by National Pharmaceutical Pricing Authority, Government of India
- Emergency Use authorization of vaccines/ drugs in pandemic situation
- Regulation of nutraceuticals, medical devices, biologics and biosimilars
- Mutual acceptability of data across countries.
- Phytopharmaceuticals.

K. Pharmacovigilance and allied topics, including:

- Types of adverse drug reactions
- Methods of pharmacovigilance
- Causality assessment
- Signal detection and processing
- Adverse events following immunization
- Haemovigilance
- Materiovigilance
- Medication errors
- National program- PvPI, WHO program of international drug monitoring.

L. Clinical toxicology, including:

- General principles of toxicology
- Common poisons and drug toxicities
- Common environmental and occupational hazards
- Basic mechanisms of mutagenesis, teratogenesis, carcinogenesis and organ-specific toxicities
- Sources of toxicology information
- General management of poisoned patient

- Use of specific antidotes and chelating agents
- Use of specialized treatment techniques e.g. charcoal haemoperfusion, haemodialysis
- Management of envenomation e.g. scorpion or snake bites
- Aspects of analytical and forensic toxicology relevant to the poisoned patient.

M. Novel drug delivery systems and therapeutic approaches, including:

- Liposomal and nanoparticle-based drug delivery
- Inhalational drug delivery
- Monoclonal antibodies and other targeted therapies
- Gene therapy
- Stem cell therapy

N. Miscellaneous topics, including:

- Biosimilar drug products
- Drug utilization studies
- Principles of evidence-based medicine
- Basics of bioinformatics
- Orphan drugs
- Basic and clinical contraceptive research for women and men
- Fetal medicine
- Critical appraisal of pharmaceutical promotional literature
- Clinical Trials Registry of India
- Role of government institutes, pharmaceutical industry, and academic centres in drug development collaborative efforts.
- Intellectual Property Rights and patent rights
- Setting up clinical pharmacology units – roles, infrastructure, personnel requirements.
- Drug repurposing/ repositioning
- Drug development during emergency situations viz. pandemics.
- Ethnopharmacology
- Reverse pharmacology
- Ecopharmacology
- Translational pharmacology
- Chronopharmacology
- Off label use of drugs
- Orphan drugs
- Structural Activity relationship of sympathomimetics, corticosteroids and Antipsychotics.
- Recent advances in cardiovascular drugs and management of HIV.

O. Analytical-biochemical assay:

- ELISA
- Radioimmunoassay (RIA)
- Fluorescence polarization immunoassay (FPIA)
- Thin layer chromatography, HPLC, PCR, GC-MS, LC-MS
- Nuclear magnetic resonance(NMR)
- High throughput screening (HTS)
- Spectrophotometery
- Limit test in pharmaceuticals, Limulus Amebocyte Lysate (LAL)
- Compartmental analysis of drug development
- Non- Compartmental and Compartmental approaches to PK/PD analysis