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PHARMACOLOGY - III

UNIT 5

TOPIC :

- **Chronopharmacology**

- a. Definition of rhythm and cycles.
- b. Biological clock and their significance leading to chronotherapy



Chronopharmacology

- Chronopharmacology is the branch of pharmacology that studies how biological rhythms (biological clock) influence the action, effectiveness, and toxicity of drugs, and how the time of drug administration affects therapeutic outcomes.
- Chronopharmacology is the study of the interaction between biological rhythms and drug action, including the effect of the timing of drug administration on drug efficacy and toxicity.
- The human body follows a natural 24-hour biological cycle (circadian rhythm). Many physiological functions such as hormone secretion, body temperature, blood pressure, sleep, digestion, and enzyme activity change throughout the day.
- Because of these daily variations:
 - Drug absorption changes.
 - Drug distribution changes.
 - Drug metabolism changes.
 - Drug elimination changes.
 - Drug response changes.
- Therefore, medicines may produce better therapeutic effects and fewer side effects when given at the correct time.
- This concept is known as Chronotherapy.

Definition of Rhythm

- A biological rhythm is a regular and predictable change in physiological, biochemical, or behavioral activities occurring repeatedly over a specific period of time.

Examples

- Sleep–wake cycle
- Body temperature rhythm
- Heart rate rhythm
- Blood pressure rhythm

Definition of Biological Cycle

A biological cycle is the repeated sequence of biological events occurring at regular time intervals under the control of the body's biological clock.

Examples include:

- Sleep cycle
- Menstrual cycle
- Circadian rhythm
- Seasonal rhythm

Types of Biological Rhythms (Cycles)

1. Circadian Rhythm

→ Circadian rhythm is a biological rhythm with a cycle of approximately 24 hours.

Examples

- Sleep–wake cycle
- Cortisol secretion
- Melatonin secretion
- Blood pressure variation
- Body temperature variation

Significance

- Most important rhythm in chronopharmacology.
- Controls daily physiological activities.
- Determines the best time for drug administration.

2. Ultradian Rhythm

→ Ultradian rhythms occur more than once within 24 hours.

Examples

- Heartbeat
- Respiration
- Hunger cycles
- REM sleep cycles

3. Infradian Rhythm

→ Rhythms with a duration longer than 24 hours.

Examples

- Menstrual cycle
- Pregnancy
- Seasonal hormone changes

4. Circannual Rhythm

→ Rhythms occurring once every year.

Examples

- Seasonal allergies
- Seasonal depression
- Animal hibernation

BIOLOGICAL CLOCK

- The biological clock is the body's natural internal timing system that regulates physiological and behavioral activities according to a regular daily cycle.
- It synchronizes body functions with environmental changes such as day and night.

Location of Biological Clock

- The main biological clock is present in the Suprachiasmatic Nucleus (SCN) of the Hypothalamus in the brain.
- The SCN receives information from the eyes about light and darkness and controls the body's circadian rhythm.

Factors Affecting Biological Clock

- Light and darkness
- Sleep habits
- Shift work
- Jet lag
- Stress
- Age
- Food intake
- Physical activity

Functions of Biological Clock

The biological clock regulates:

- Sleep and wakefulness
- Hormone secretion
- Body temperature
- Blood pressure
- Heart rate
- Digestion
- Metabolism
- Immune function
- Cell division

Significance of Biological Clock

1. Regulates Sleep

- Maintains a normal sleep–wake cycle.

2. Controls Hormone Release

- Regulates hormones such as cortisol, melatonin, insulin, and growth hormone.

3. Regulates Blood Pressure

- Blood pressure is highest in the morning and lower during sleep.

4. Controls Drug Response

- Drug efficacy and toxicity vary according to the time of administration.

5. Maintains Body Temperature

- Body temperature changes throughout the day.

6. Improves Treatment Outcome

- Correct timing of medicines improves therapeutic response and reduces adverse effects.

Chronotherapy

→ Chronotherapy is the administration of medicines at the most appropriate time according to the body's biological rhythm to maximize therapeutic benefit and minimize adverse effects.

Principle of Chronotherapy

Drug administration should coincide with the body's biological rhythm and the timing of disease symptoms.

Correct timing results in:

- Better efficacy
- Reduced toxicity
- Lower drug dose requirement
- Improved patient compliance

Importance of Chronotherapy

- Improves therapeutic effectiveness.
- Reduces side effects.
- Increases patient safety.
- Enhances quality of life.
- Decreases treatment failure.
- Optimizes drug concentration.
- Reduces hospital admissions.

Applications of Chronotherapy

1. Hypertension

Blood pressure rises early in the morning.

Drug timing:

- Long-acting antihypertensive drugs are often given at bedtime to control early morning blood pressure.

2. Asthma

Asthma attacks are more common during the night and early morning.

Drug timing:

- Bronchodilators and corticosteroids are often administered in the evening.

3. Rheumatoid Arthritis

Joint stiffness and pain are worse in the early morning.

Drug timing:

- NSAIDs or corticosteroids are administered at night so that maximum effect occurs in the morning.

4. Peptic Ulcer

Gastric acid secretion is highest during the night.

Drug timing:

- Proton pump inhibitors or H₂ blockers are usually taken before meals or at bedtime depending on the drug.

5. Hypercholesterolemia

Most cholesterol synthesis occurs at night.

Drug timing:

- Short-acting statins (e.g., Simvastatin) are usually taken in the evening.

6. Cancer Chemotherapy

Some anticancer drugs are more effective and less toxic when administered at specific times according to cell cycle rhythms.

7. Diabetes Mellitus

Insulin and oral antidiabetic drugs are timed according to meal patterns and blood glucose fluctuations.

Advantages of Chronotherapy

- Better drug efficacy.
- Reduced adverse effects.
- Lower drug toxicity.
- Improved patient compliance.
- Improved disease control.
- Reduced healthcare costs.
- Personalized treatment approach.

Limitations of Chronotherapy

- Individual biological rhythms differ.
- Requires strict adherence to dosing schedules.
- Difficult in emergency situations.
- Limited evidence for some diseases.
- Not applicable to all medications.