

# CHRONOBIOLOGY & CHRONOTHERAPY



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Chronobiology is defined as the study of the time related events shaping our daily biologic responses. It may applied to any respect of medicine dealing with alteration of pathophysiology and treatment responses.

Regulation of medication according to **CHRONOBIOLOGY** is known as **CHRONOTHERAPY**. The philosophy is explained as below:

## A. RESPIRATORY SYSTEM

**Asthma** : During the day, bronchial patency increases and peaks at around 4 p.m. and decreases during sleep. Endogenous corticosteroids are at their lowest level around midnight. Thus at 3 p.m. dose of oral corticosteroids are more effective. Single night-time dose of theophylline for nocturnal bronchospasm and evening dose of beta-agonist are better than other times.

## B. CARDIOVASCULAR SYSTEM

Blood pressure and heart rate, serum catecholamines, plasma renin, angiotensin and aldosterone, hemoglobin, hematocrit, platelet aggregations and viscosity are maximum in the morning hours

whereas tPA levels are low.

- i) Myocardial ischemia is most frequent during first few hours after arousal. Thus Aspirin is given in the morning to give its maximum antiplatelet effect. But thrombolytics and heparin have minimal benefit in the early morning hour.

Long acting nitrates in the morning decrease ischaemic activity as well as reduce occurrence of tolerance.

Beta blockers and Ca-channel blockers attenuate the circadian pattern of ischaemic events.

## ii) Hypertension

Betablockers: Atenolol decreases daytime blood pressure but nocturnal and early morning surge is insignificantly reduced.

ACE inhibitors; Enalapril has peak effect in the morning after an evening dose.

Diuretics: Frusemide given at 9.00 p.m. leads to more urine volume, sodium and chloride excretion than at 9.00 a.m. (during first hour)

## C. ORGAN REJECTION & IMMUNOSUPPRESSION

Immunological activity is at its peak at night time while immunosuppressives are given during the day. Most organ rejections are

to occur around 6.00 a.m. Therefore, it seems logical to give maximum immunosuppression at night.

#### D. GASTROENTEROLOGY

Gastric mucosal defence against Aspirin is low when given at 8.00 a.m. and 8.00 p.m.

Gastric acid secretion is higher in the evening especially in ulcer patients. So II 2 receptor blockers are more effective at night.

#### E. ARTHRITIS

Early morning inflammation (pain) is more in Rheumatoid Arthritis. NSAID in twice a day large dose especially one dose at night is more effective than 4 small doses.

Osteoarthritis pain worsens as the day proceeds. So pain relievers if given before the onset of pain is more effective.

#### F. ANTIMALARIAL

*P. falciparum* when treated with chloroquine, ring to young trophozoite forms are noted to be refractory. Animal model shows that two doses 18 hours apart, with first dose at maximum mid-size trophozoite stage in peripheral smear gives best results.

#### REFERENCES

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