

Evaluating the Clinical Significance of Chronopharmacology in Patients Admitted to the General Medicine Department

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ABSTRACT

Aim and Objectives: To study the Chronopharmacological relevance to the time of drug administration in the patients admitted in General Medical Ward. Assess the clinical impact of chronopharmacology in patient care. **Methodology:** It is a Prospective Observational Study and the data was obtained from the patient's case reports, prescriptions and by direct interacting with the patients admitted in General Medical ward over a period of 6 months- from November 2021 to April 2022. **Results and Discussion:** The study includes 282 study subjects of both genders based on the inclusion criteria. In this study we evaluated the relevance of Chronopharmacology and clinical outcomes. As the adherence to Chronopharmacology increases the better will be the Clinical outcome and reduces the chance of drug toxicity, there by increases the patient's quality of life. **Conclusion:** The Chronopharmacological knowledge and inclusion of this concept in the prescription of medicine is the crucial to achieve better clinical outcome and chances of drug toxicity are reduced and duration of the hospital stay is also reduced and improves the patient's quality of life.

Keywords: Chronopharmacology, Therapeutic Efficacy, Clinical Outcomes, Patient Care, Circadian Rhythms

INTRODUCTION:

Chronopharmacology is the investigative science that elucidates the biological rhythm of medications. Chronopharmacology minimizes the adverse effects of the drug by optimizing the drug-effects through administration of the drug related to the Biological rhythm. Chronopharmacokinetic studies of many drugs attempt to explain chronopharmacological phenomenon and demonstrate that the time of administration is a possible factor of variation in the pharmacokinetics may proceed from 24 hours rhythms in each process of ADME. Hence the quantitative as well as qualitative response of an organism varies with the time of drug administration

Many disease patterns changes according to physiological changes. It also a very important in influencing the responses to various medications. The disease occurrence is independent of time of day, month or year. The concept of biological rhythm is important constancy in the blood concentration of drugs so as to maintain the constant efficacy of drug. The circadian time has to be taken into account as an important variable influencing a drugs pharmacokinetics and its effector side effect. Applying the knowledge of circadian function and regulation to the relevance of disease has enabled a chronotherapy approach in the timing of administration of conventional drugs to synchronize the rhythms in disease activity with the efficacy of the drug.

The goal of chronopharmacology is as follows:[5]

- Optimization of therapy by considering rhythm dependencies.
- Prevention of overdosing and unnecessary side effects of any class of drugs.
- Prediction of time variability in manifestation and severity of diseases.
- Matching the timing of treatment with intrinsic timing of illness.
- Thus improve efficacy and safety of medications.

Chronopharmacology of different drugs:

The anti-hypertensive drug kinetics also changes with circadian rhythm. When the drug is administered in the Morning the peak plasma concentration of the drug (C_{max}) is more and the time to reach the maximum C_{max} (t_{max}) is less which differs in the case of lipophilic drugs. The HMGCO-A reductase enzyme also known as Statins is given at the Night for the better control of cholesterol synthesis (6).

As symptoms of rhinitis are heightened during the morning and evening so the administration of a Non-sedative Anti-histaminic drugs before going to bed is beneficial and also reduces the disturbances during sleep (7). Drugs like Theophylline and Etophylline are administered at Bed-time by this we can improve the symptoms of Asthma and also decreases the drug toxicity by avoiding multiple-dose administration. The secretion of gastric acid is more during the Evening and at Night in order to control the acid secretions, the bed time administration of drugs like H2 blockers (once daily) is more preferable and Proton pump Inhibitor (PPI)like Pantoprazole, Lansoprazole and Omeprazole are administered in the morning (8).

The cancer drugs are administrated based on the duration of the phase of the cell cycle and Cell proliferation rate. For example In the case of colorectal cancer::The administration of 5-Flourouracil (5-FU) is preferred at night-time whereas Oxaliplatin is preferred in the morning

(19).The tolerance of cisplatin is better around 4.00 pm to 8.00 pm and evening administration shows decreased renal toxicity of the cisplatin.

AIM:

- To evaluate the Chronopharmacology relevance of medicines and its impact on clinical outcomes in General Medical Ward.

OBJECTIVES:

- To study the Chronopharmacological relevance to the time of drug administration in the patients admitted in General medicine ward.
- Assess the clinical impact of chronopharmacology in patient care.
- Observing and recording the time of drug administration in relation to the circadian rhythm.
- Evaluate the relevance of chronopharmacology.

METHODOLOGY:

Study design and selection criteria: A Prospective Observational study was conducted in the Department of General Medicine, Government General Hospital, Ananthapuramu, Andhra Pradesh for a period of 6 months from November 2021-April-2022 with a sample size of 282 Patients admitted in General Medicine wards of age group 14 years and above of either gender for chronic disease conditions were included in the study. Patients receiving emergency treatment in the wards of General Medicine and Pregnant Women were excluded from the study.

Study procedure: A Pilot study was conducted in the General Medicine Department of Government General Hospital of Ananthapuramu. A study of total 282 patients were enrolled in the study based on Inclusion and Exclusion Criteria. The research protocol is explained to the Patient and Patient representative and the information is collected who gave Consent orally. From the collected data, the Prescription drug dose, Dosage, Dosage regimen and Frequency and Time of administration was analysed with the help of ASHP (American Society of Health system Pharmacists) textbook, BNF (British National Formulary), Micromedex database, Medscape and Literatures in order to check the Clinical relevance of Chronopharmacology.

Source of Data collection: Information of the patients is collected from case sheets in General Medicine Department. Complete case sheets, Prescription and Direct interaction with the patient **Statistical analysis:** All the collected data were entered into the Microsoft Excel and performed a descriptive statistic. The Statistical software called Graph pad version 3.10, 2009 is used to perform Statistical tests namely Odds ratio and Pearson's correlation coefficient. Odds ratio was performed to identify the significance of Gender wise distribution of the prescriptions follows Chronopharmacology guidelines. Pearson's correlation coefficient was used to identify the Relationship between Chronopharmacology and Clinical outcomes. The P-value <0.05 was considered statistically significance.

Results:

A total of 300 patients are screened for the collection of the data in General Medicine Department of Government General Medicine, in that 282 patient met the inclusion criteria and included into the study.

Socio-demographics details:

Among 282 patients the Male patients are 134(47.5%) and Female patients are 148(52.5%) (Table: 5.1) and the average age of both males and females found between 17 years and 85 years (Table: 5.2).The Mean average age is 57 year.

(Table-5.3)Represents Total Drugs included in our study to assess the chronopharmacology. In this study, a total 1326 drugs are collected in the General Medicine department of Government General Hospital. In that, 808 (60.9%) drugs show relevance to chronopharmacology guidelines in their administration and 512 (39.1%) drugs doesn't show relevance to chronopharmacology guidelines in their administration.

(Table:5.4) Represents Gender wise distribution of Prescriptions included in the study. In total 282 prescriptions, the prescriptions of Males show 107(79.8%) relevance to Chronopharmacology and the Prescriptions of Females show 105(70.9%) relevance to chronopharmacology.

(Table:5.5) Represent Relation between Chronopharmacology and Clinical Outcome. In total 282 , 212(75.1%) shows adherence to chronopharmacology in that 164(77.3%) shows improved clinical outcome along with 48(64.3%) doesn't show improvement in clinical outcome and 70(24.9%) shows nonadherence to Chronopharmacology , in which 25(35.7%) shows improved clinical outcome whereas 45(64.3%) doesn't show improvement in clinical outcomes.

DISCUSSION:

This study includes 282 study subjects among 134(47.5%) were Males and 148(52.5%) were Females. Where as in previous study they included 744 study subjects in which 506 (68.10%) were Males and 238 (31.90%) were Females (9).

In current study, the age of the patients ranged from 17years to 85years.The patients were in the age 17-40 age – 55(19.5%);41-70 age-174(61.7%) and >70 years age(18.8%).The Mean average age is 57 years. In previous study the mean average was 55years (10).

The aim of the study is to evaluate the to evaluate the Chronopharmacology relevance of medicines and its impact on clinical outcomes in General Medical Ward of Government General Hospital, Anathapuram. We have tried to evaluate the prescriptions that show clinical relevance to Chronopharmacology to obtain better clinical outcomes. In a total of 282 prescriptions, 212 (75.1%) prescription show relevance to Chronopharmacology guidelines and 70 (24.9%) prescription doesn't show relevance to Chronopharmacological guidelines. The Prescriptions of Males displays more relevance to Chronopharmacology than that of the Prescription of Females in General Medicine Department.

A study on “Chronopharmacology and drug prescribing pattern of physicians in a tertiary care hospital of North India” stated that the drug prescriptions mainly Statins, Proton pump inhibitors, Beta-blockers and Insulin shows correlation with the Chronopharmacological pattern to achieve better benefit from the medications (11-14). In our study we evaluated the relation between Chronopharmacology and Clinical outcomes, which states that a better Chronopharmacological adhered prescriptions will results in a better clinical outcome.

The contributing factors for poor clinical outcome may be Medication adherence, Lifestyle changes, Family history.

A study conducted by Pichholiya M et.al., on “Knowledge and practices of Chronotherapeutic among health-care professionals in a tertiary care teaching institute of South Rajasthan” (15) shown that the prescription of medications with correlation of chronopharmacology without familiar with the term chronopharmacology by the significant number of the experienced faculty as compared to the residents.

The current study adds scope for improvement in the therapeutic outcome if chronopharmacology is considered in treatment as the physiological activities in the body adhere to this circadian rhythm to produce a normal homeostasis. In view of the current research and investigations, the chronopharmacologic aspect plays a major role for the optimal utilization of the available drugs to fetch an improved therapeutic effect when followed in clinical practice.

This study also highlights the timing of drug administration of existing and new drug substances importance in human health which acts on the peripheral clock which in turn helps us to establish more appropriate Chronopharmacologic and Chronotherapeutic approaches.

CONCLUSION:

To show the good clinical relevance of standard Chronopharmacology, the timing of drug administration is the major factor to be considered. The chronopharmacological knowledge and inclusion of this concept in the prescription of medicine is the crucial in understanding interaction between biological clock and drug for an effective therapy in order to achieve better clinical outcomes and chances of drug toxicity is reduced and duration of the hospital stay is also reduced and improves the patient quality of life. The current study adds a scope for improvement in the therapeutic outcome if chronopharmacology is considered in the treatment. Future Prospective Newer drug delivery systems are presently in the vogue. These drugs are called as chronopharmaceuticals. Chronopharmacology applied to different drug delivery systems, and their beneficial effects could be studied in the future (3).

Limitations of the Study:

The current study has involved only the patients admitted in the General Medical department of the tertiary care hospital where the drugs are minimally available and the study mainly focused on the timing of the drug administration. The present study didn't account the importance of treatment based on the Chronopharmacologic relevance in case Paediatric patients and also in case of Emergency situations. The study didn't take into account the dose of each drug and dosage form. Also the beneficial effects of chronopharmaceuticals. This could be addressed in the future studies in the field.

Table: 5.1: Demographics- Gender wise distribution:

Gender	No of the patient	Percentage
Female	148	52.5%
Male	134	47.5%
Total	282	100%

Table:5.2: Age wise distribution (Minimum-16 years and Maximum 85 years)

Age	Number of patients	Percentage
17-40 years	55	19.5%
41-70 years	174	61.7%
>70years	53	18.8%
Total	300	100%

Table 5.3: Total Drugs included in our study to assess the chronopharmacology (n=1326)

No.of following Chronopharmacology	No.of prescriptions does not shows chronopharmacology
808(60.9%)	512(39.1%)

Table -5.4- Gender wise distribution of prescriptions included in the study (n=282)

Gender	Number present	No of Prescriptions followed chronopharmacology guidelines		Odds Ratio	P Value
		Followed (%)	Not followed (%)		
Male	134	107(79.8%)	27(20.2%)	1.623	0.0980
Female	148	105(70.9%)	43(29.1%)		

Figure 5.1

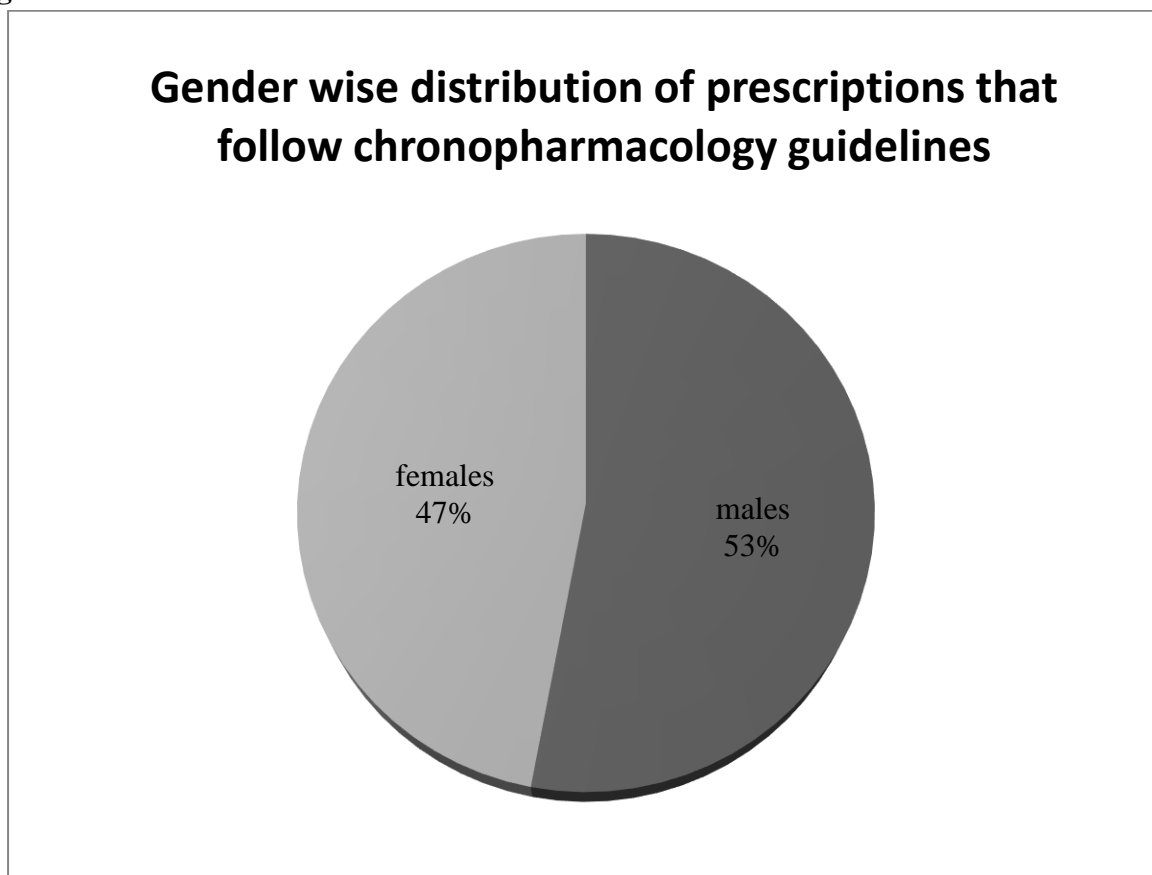
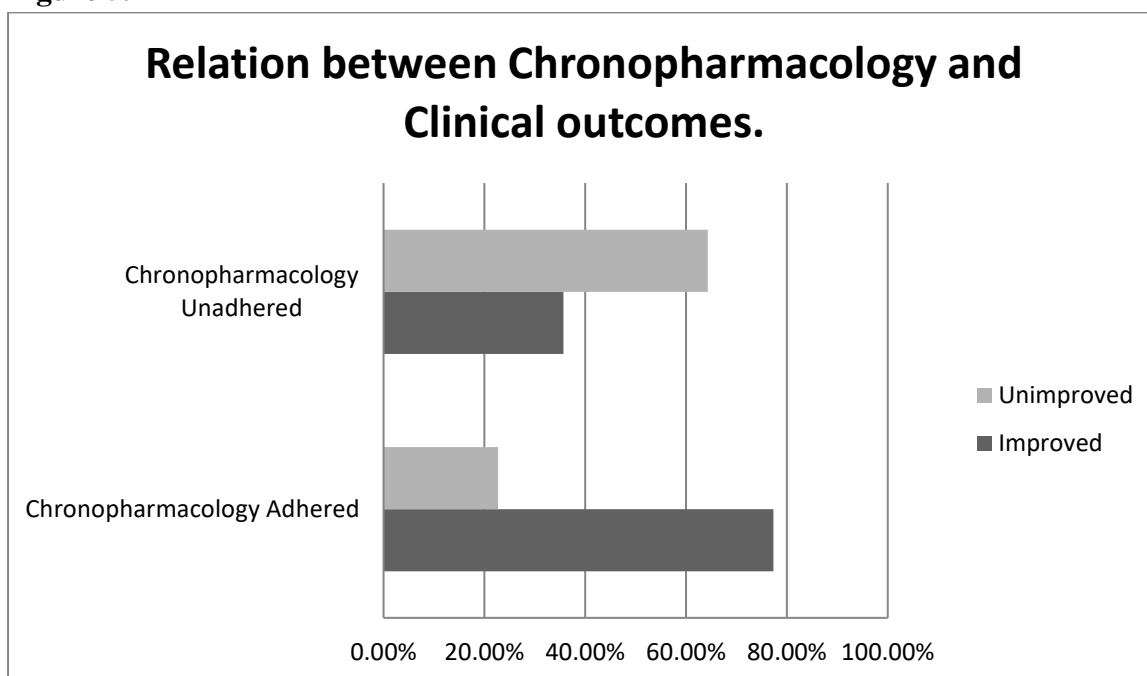


Table 5.5: Relation between Chronopharmacology and Clinical Outcomes

Chronopharmacology	Percentage	Clinical outcomes		Correlation co-efficient(r)	P-value
		Improved	Unimproved		
Chronopharmacology Adhered	212(75.1%)	164(77.3%)	48(22.7%)	0.3826	<0.0001
Chronopharmacology Un adhered	70(24.9%)	25(35.7%)	45(64.3%)		

Figure 5.2



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