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Evaluation of Knowledge and Practice of Chronopharmacology among Medical and Dental Resident Doctors from a Teaching Hospital

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ABSTRACT

Background: Chronopharmacology focuses on how biological rhythms, particularly circadian rhythms, affect the pharmacokinetics and pharmacodynamics of medications. Understanding these principles is essential for optimizing drug efficacy and minimizing adverse effects. Despite its importance, knowledge and practical application among resident doctors remain limited. To assess the understanding and application of chronopharmacology among healthcare-related and dental resident doctors.

Methods: A cross-sectional questionnaire-based study was conducted among 200 resident doctors from both medical and dental departments at a tertiary care teaching hospital in Visakhapatnam. A structured and validated 12-item questionnaire (8 knowledge-based, 4 practice-based) was shared via digital platforms. Data on demographics, knowledge, and practice regarding chronopharmacology were collected and analyzed using descriptive statistics.

Results: Among the participants, 60% were medical and 40% dental residents. While 90% understood that chronopharmacology concerns drug effects on biological rhythms, only 51% recalled formal training during their education. Most participants (97%) reported educating patients about the timing of drug intake, and 82% acknowledged that therapeutic efficacy and toxicity vary with administration time. However, only 42% had observed therapeutic failure due to improper timing.

Conclusion: The findings reveal satisfactory conceptual awareness but limited formal education and clinical integration of chronopharmacology among resident doctors. These results support the need for curriculum enhancement and continuing education initiatives in chronotherapeutics for better patient care.

Key-words: Chronopharmacology, Circadian Rhythm, Drug Therapy, Healthcare Professionals and Knowledge Assessment

INTRODUCTION

The human body exhibits notable variations in biological functions over 24 hours, referred to as the circadian rhythm, which is influenced by the sleep-wake cycle [1].

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Circadian rhythms are regulated by a system of primary biological clocks in the brain and peripheral clocks present in various tissues. Chronobiology is the field dedicated to the examination of biological rhythms and their underlying mechanisms. The field of chronobiology that investigates how medication influences the timing of the biological interplay of events and rhythms and their interrelation of biological chronometry, with the impact of drugs, is called chronopharmacology. Chronotherapy refers to the therapeutic use of chronopharmacology. It incorporates chrono-pathological, chrono-pharmacology, and chrono-

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toxicological data to improve a drug's efficacy and tolerance of medication by identifying the most suitable administration times based on circadian rhythms. This can be achieved by administering conventionally formulated dosage forms at the correct times and unique pharmaceutical distribution mechanisms (Chrono formulations) to align medication levels with circadian rhythms of disease activity [2]. Chronotherapy requires a comprehensive understanding of circadian classification in terms of the intensity of disease manifestations and consistent trends in the human body's pharmacokinetics, which govern drug therapeutics and lateral effects [3].

To promote the rational use of medicines, the World Health Organization (WHO) has established guidelines that advocate for patients to be educated about their medications, comprehend the significance of the prescribed therapies, and adhere to the treatment regimen of drugs as necessary and in the appropriate manner time [4]. Recently, it has been identified that even dental or oral tissues show circadian rhythms, which can be important in treating a few dental diseases. So, dental resident doctors are also included in this study. Circadian rhythms are biological cycles that span 24 hours and regulate numerous physiological functions within the body [5]. These patterns are orchestrated through an internal "clock" – the suprachiasmatic nucleus, a critical component of the circadian rhythm regulation (SCN) in the hypothalamus – that aligns with environmental cues like light and dark cycles [6]. The SCN functions as a primary pacemaker, coordinating biological cycles that follow 24 hours throughout the brain and peripheral organs.

Various physiological functions, such as sleep-wake cycles, body temperature regulation, and hormone secretion, are governed by circadian rhythms, and metabolism exhibits circadian rhythms. Disruptions to these rhythms can have significant health consequences. For instance, the severity of conditions like asthma and rheumatoid arthritis can vary throughout the day, and acute events like myocardial infarction are more likely to occur at specific times [7–13].

The basis for chrono dentistry has been set by showing evidence of peripheral timekeeping mechanisms within the dental pulp, periodontal structures, oral mucosa, enamel, dentin, and mandibular bone. Abnormal clock mechanisms have been linked to the progression of oral cancer and juvenile skeletal mandibular hypoplasia [14].

Chronotherapy recognizes the impact of circadian pharmacological rhythms' efficacy as well as toxicity. By dispensing pharmaceuticals at designated intervals that synchronize with the body's inherent rhythms, we can optimize treatment outcomes while minimizing side effects. This approach involves understanding the influence of circadian rhythms on the processes of drug absorption, distribution, metabolism, and elimination, as well as their effects on target tissues. Several clinical applications of chronotherapy have been explored. For example, administering cholesterol-lowering medications at bedtime can enhance their effectiveness. Similarly, timing asthma medications to coincide with peak symptom periods, typically at night, can improve symptom control. The proper knowledge about chronotherapy and chronopharmacology among doctors is essential in medical practice. This study mainly aims to evaluate the knowledge about chronopharmacology and its implications in medical or dental practice in resident doctors.

MATERIALS AND METHODS

Study Design and Setting- This is an observational cross-sectional questionnaire-based study conducted at a university in Visakhapatnam, Andhra Pradesh, India. The data was collected over two months, November and December 2023.

Study Population- The study population included senior and junior resident doctors working in medical and dental departments. Postgraduates from General Surgery, General Medicine, Pediatrics, Anaesthesia, Dermatology, Psychiatry, Social and Preventive Medicine, Obstetrics and Gynaecology, Orthopaedics, and Radiology were included in the medical college. Postgraduates from Orthodontics, Conservative Dentistry, Prosthodontics, Periodontics, Pedodontics, and Oral Surgery were included in the dental college.

Data Collection Method- Resident doctors were personally approached in the hospital. Study objectives were explained, and a pre-tested and validated questionnaire was shared via WhatsApp or email in Google Forms format. Demographic data such as designation, department, and gender were collected. The questionnaire consisted of 12 questions—8 to assess knowledge and 4 to assess practice.

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Informed Consent and Confidentiality- The research was conducted following the acquisition of informed consent from the resident doctors. All information collected was kept confidential.

Sample Size- The questionnaire was shared with 200 medical and dental resident doctors. This number was derived based on a previous study conducted in Rajasthan.

Statistical Analysis- The information collected was analyzed and presented using percentages.

Ethical Approval- This study was conducted after obtaining approval from the Institutional Ethics Committee.

RESULTS

A total of 200 resident doctors participated in the study, 120 (60%) from the medical and 80 (40%) from the dental postgraduate departments. Females comprised 65% of the participants, and males comprised 35%. 63% of the study participants were junior residents, and 37% were senior residents. The results for the knowledge component of the questionnaire came out like this. 80% (160) of the participants responded correctly to the question regarding the main center for circadian rhythms in the brain. The data regarding this question is shown in Fig. 1

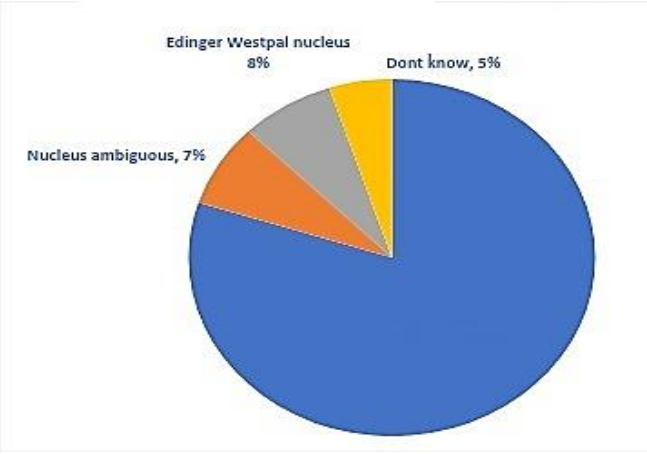

Fig. 1: Pie diagram showing participants' knowledge of the center for circadian rhythms

The suprachiasmatic nucleus, a critical component of circadian rhythm regulation, generates and synchronizes biological clocks in our body. 75% of the participants opined that the core body temperature, cardiovascular function, and hormone secretions display circadian rhythms in our body. 25% of them opted for only one of the above options as the correct answer. Only 68% of the participants responded correctly that at the molecular scale, the circadian rhythm clock is based on the functioning of circadian rhythm genes. This data is depicted in Fig. 2.

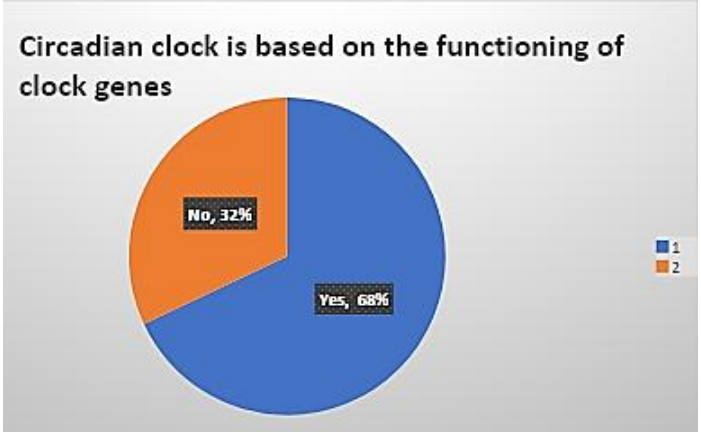

Fig. 2: Pie diagram showing participant's knowledge of clock genes

90% of the resident doctors opined, "chronopharmacology is concerned with the effects of drugs on the timing of biological events and rhythms". This data is shown in Fig. 3.

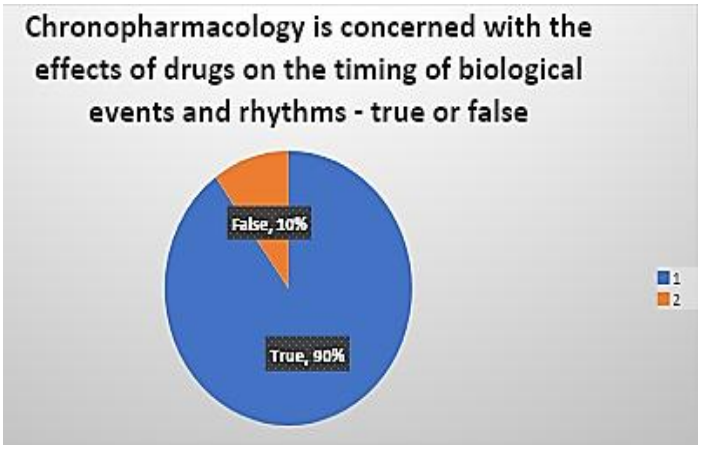

Fig. 3: Pie diagram showing participant's knowledge of the effects of drugs on the timing of biological events and rhythms

82% of the doctors responded positively to "Circadian rhythms can affect therapeutic efficacy and toxicity based on the dosing time". This data is shown in Fig. 4.

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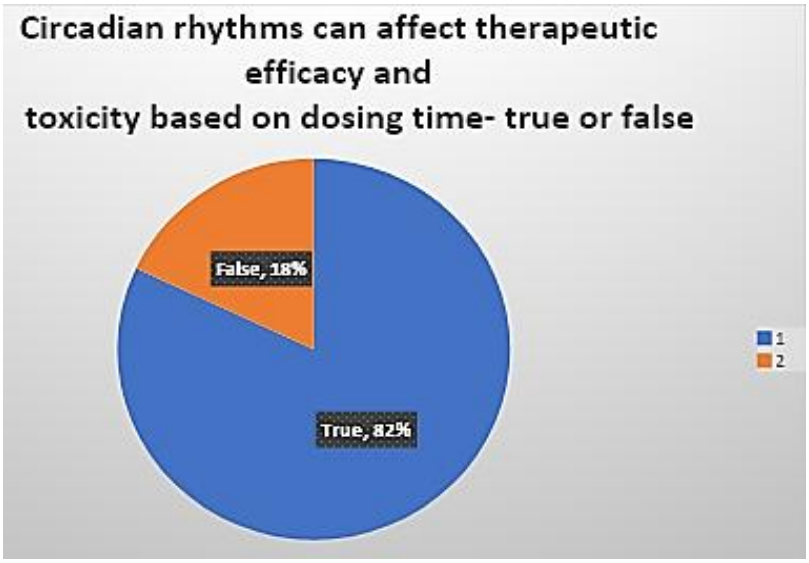

Fig. 4: Pie diagram showing knowledge that Circadian rhythms can affect therapeutic efficacy and toxicity based on dosing time- true or false

The complete data regarding the knowledge aspects of questions is given in Table 1.

Table 1: Participants' answers to questions on the Knowledge of Chronopharmacology

Questions on Knowledge	Correct responses (%)
1. The circadian rhythm in the human body is generated, controlled, and synchronized by the nucleus in the brain (multiple choice question)	80% (160)
2. Which of the following physiological functions of the body display circadian rhythms? (multiple choice question)	75% (150)
3. At the molecular level, the circadian clock is based on the functioning of clock genes - true or false	68% (136)
4. Chronopharmacology is concerned with the effects of drugs on the timing of biological events and rhythms - true or false	90% (180)
5. Chronotherapeutics is an area where the dosing regimen is synchronized with biological rhythms - true or false	83% (166)
6. Circadian rhythms can affect therapeutic efficacy and toxicity based on dosing time- true or false	82% (164)

Chronotherapy is important in the treatment of the condition's hypertension, acute coronary syndrome, ventricular arrhythmias, migraine, adrenal insufficiency, clinical dentistry hyperlipidemia, cancer, and bipolar disorder. Study participants can choose more than one option for this question, and all the options have corrected answers. The results for this question are depicted in Fig. 5.

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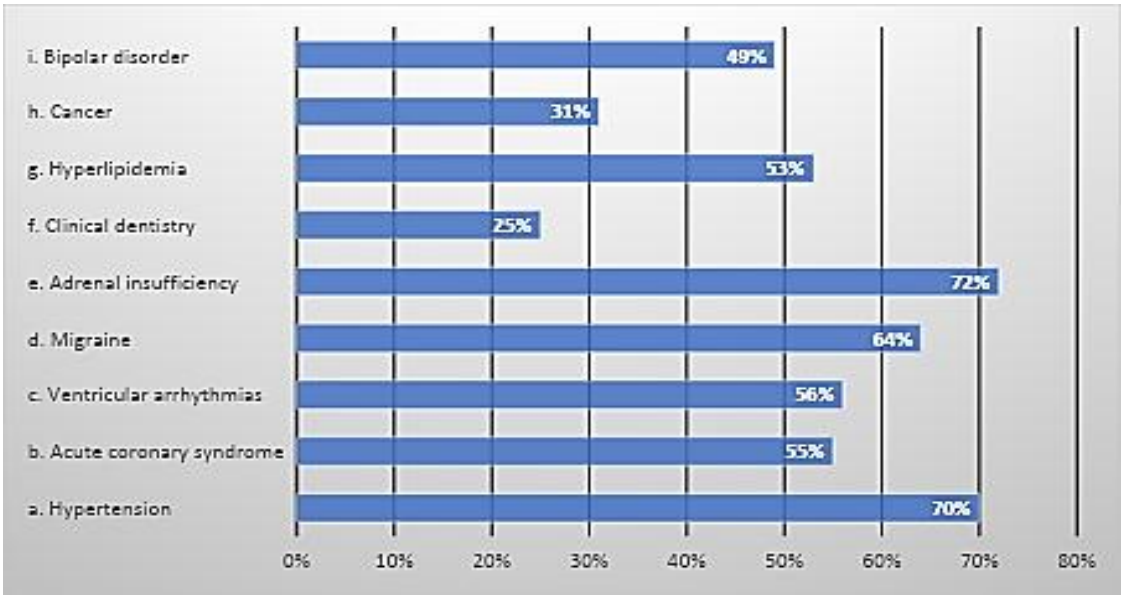

Fig. 5: Percentage of responses for the importance of chronopharmacology in the treatment of disease.

The results for the practice aspects of the questionnaire came out like this. 42% (84) of the study participants faced a scenario in which the prescribed medication proved insufficiently effective owing to improper timing of administration. Effective patient education concerning the time administration of pharmaceuticals was a crucial component of the clinical application of skills for 97% (194) of the study participants. This data is depicted in the pie diagram Fig. 6.

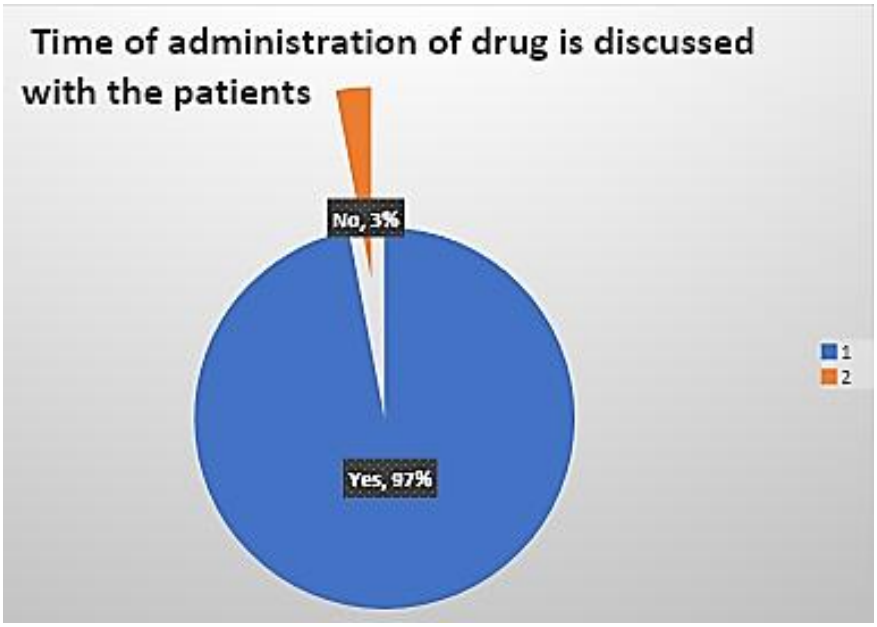

Fig.6: Pie diagram showing participant's practice method – time of administration of the medicine is discussed with the patients.

78% (156) of the participant's opined that Chronotherapy has the potential to mitigate the negative side effects associated with medication. Eighty-one percent (162) of the study individuals involved agreed that the study of chronotherapy can enhance the effectiveness of a pharmaceutical agent. 51 % of the individuals involved in the study only remember that chronopharmacology was taught during their medical education; this data is shown in Fig. 7.

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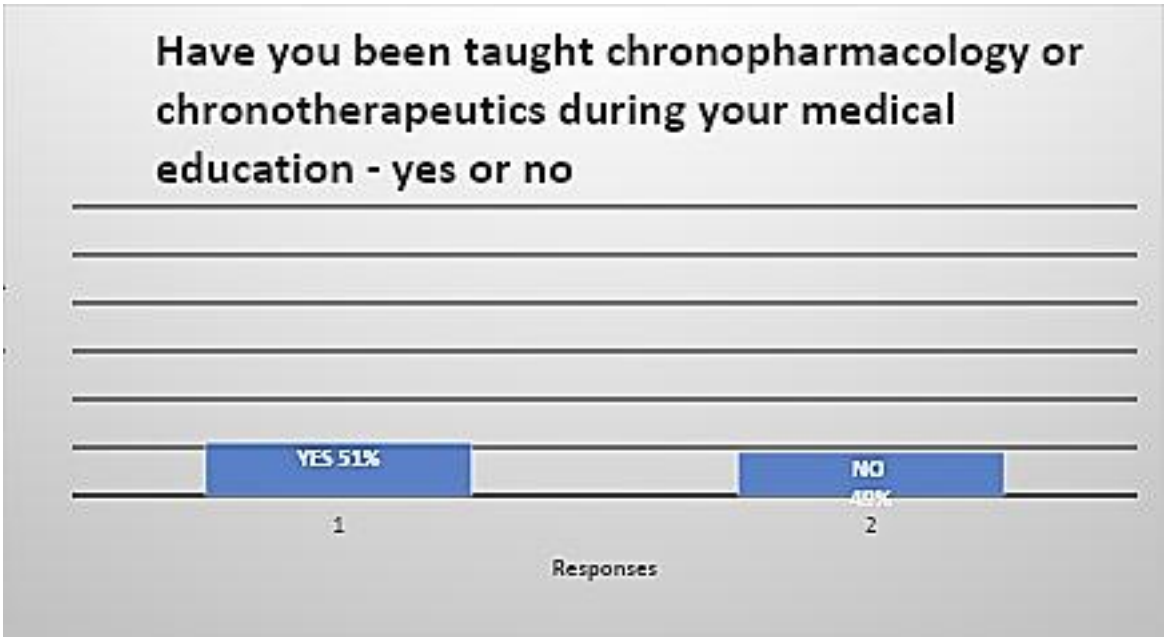

Fig.7: diagram showing participant's response to Chronotherapy education

The compiled data regarding the practice aspects of chronopharmacology is projected in Table 2.

Table 2: Participants' answers to questions on the practice of Chronopharmacology

Questions on Practice	Positive (yes) responses (%)
Have you ever encountered a situation where the drug prescribed was not effective enough due to incorrect timing of intake? - yes or no	42% (84)
Correct timing of drug administration is always mentioned in your prescription - yes or no	84% (168)
Proper patient counseling regarding the time of drug intake is an essential part of your practice- yes or no	s97% (194)
Have you been taught chronopharmacology or chronotherapeutics during your medical education - yes or no	51% (102)
Chronotherapy could reduce the incidence of adverse drug effects.	78% (156)
Chronotherapy will increase the efficacy of a drug.	81% (162)

DISCUSSION

The circadian rhythm received an updated recognition when the 2017 Nobel Prize in Physiology or Medicine was conferred upon Jeffrey Hall, Michael Rosbash, and Michael Young in recognition of their research into the molecular mechanisms that regulate circadian rhythms. The central circadian clock is situated within the suprachiasmatic nucleus and obtains light-induced signals from retinal photoreceptors. This primary clock regulates the activities of the entire body by secreting hormones like melatonin, glucocorticoids, and chemical messengers.

Circadian rhythm disturbances exhibit a strong correlation with the adverse effects of shift work on health. The circadian rhythm is also relevant to vaccination. In a study comparing antibody titers after influenza vaccinations administered in the morning versus the afternoon, researchers found that individuals vaccinated in the morning exhibited a more robust antibody response. In the field of oncology, the advantages of chronotherapy in treating malignant tumors were seen. This was demonstrated for oxaliplatin, fluorouracil, and leucovorin. Better patient

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responses and treatment tolerance in cases of metastatic colorectal cancer were observed [15].

The idea of chronopharmacology is to establish the appropriate time for administering a pharmaceutical agent designed to improve effectiveness and safety, inhibit tolerance development, and reduce adverse impacts of the specified treatment. This can be accomplished by modifying the timing of the delivery of standard treatment. Drawing from the principles of chronopharmacology, the timing of ingestion and the efficacy of the drug are associated with the human biological clock body [1].

A similar study was conducted on the understanding and application of chronotherapeutics among healthcare experts from diverse clinical specialties within a tertiary care educational institution located in the southern region of Rajasthan [15]. The study participants were both teaching faculty and resident doctors, whereas, in the present study, only junior and senior resident doctors were considered. 58% of the study participants in their study were previously unfamiliar with the concepts of chronopharmacology and chronotherapeutics. This is in similar lines with the results from this study for the question 'Have you been taught chronopharmacology or chronotherapeutics during your medical education'. 49% of the study participants in this study responded that they had not been taught chronopharmacology.

45% of faculty and 50% of the residents indicated that chronopharmacology pertains to the influence of medications on the scheduling of biological occurrences and the patterns of biological rhythms in their study. These numbers are slightly different from the findings of the current research. 90% of the participants agreed with the above fact in the present study. 100% of faculty and 95% of the residents indicated that appropriate patient care counselling regarding the timing of medication administration is a critical aspect of their professional practice in their study. These statistics are almost like the 97% attained in our study. The variations in the results may be attributed to the geographic difference. The data was collected from senior faculty too in their study but in the present study, only senior and junior resident doctors were included.

Another study was conducted in Libya regarding the 'Assessment of Libyan Pharmacists' Understanding of Chronopharmacology about Antihypertensive Medications'. Their study was a descriptive cross-sectional questionnaire-based study. They collected data from pharmacies in the major cities of Libya. About 600 questionnaires were distributed to the pharmacies, and the pharmacists were requested to select the antihypertensive medications focused on in this research that were administered in the morning and evening bedtime. They concluded half of the pharmacists who participated in the study were unfamiliar with the principles of chronopharmacology and chronotherapy for antihypertensive drugs [1].

CONCLUSIONS

The importance of chronotherapy in clinical practice is always looked down upon. This performs a significant function in the promotion of prudent utilization of pharmaceuticals. Proper timing of drug intake helps improve the patient's clinical conditions with less scope for therapeutic failure and adverse effects of drugs. In this study, the knowledge about chronotherapy is evaluated and expressed. The study results emphasize the need for planning awareness programs for resident doctors in this discipline. This can help in better and safer patient care.

LIMITATIONS

The limitations of the present study include the small number of resident doctors who participated. The study results cannot be generalized to all doctors as this study is done in a single centre and a particular locality.

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CONTRIBUTION OF AUTHORS

Research concept- Dr K.P.Poojitha
Research design- Dr K.P.Poojitha
Supervision- Dr Syam Kumar Addepalli
Materials- Dr K.P.Poojitha
Data collection- Bathula Rakshita
Data analysis and interpretation- Dr Syam Kumar Addepalli
Literature search- Bathula Rakshita

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Writing article- Dr K.P.Poojitha
Critical review- Dr Syam Kumar Addepalli
Article editing- Dr Syam Kumar Addepalli
Final approval- Dr K.P.Poojitha

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