Medical Students' Knowledge and Awareness of Chronopharmacology: A Cross-Sectional Viewpoint

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Abstract

The way chronopharmacology studies 24-hour body rhythms helps achieve good results in therapy and reduce drug side effects. While chronopharmacological research is rising in clinical medicine, it's unclear how well medical students are aware of these principles. The purpose of this study is to review how much undergraduate medical students know about chronopharmacology. Participants were asked to complete a structured survey about their sleep rhythms, when drugs are administered and why. Initial research found that people have limited knowledge about chronopharmacology, showing it should be part of what doctors and pharmacists learn. Improving knowledge here can make a big difference in the way clinicians make decisions and treat patients.

Keywords: ***Chronopharmacology, Glucocorticoids, Circadian Rhythm, Cardiomyocyte, Glucose Metabolism, Glucocorticoid Receptor (GR), Heart Metabolism, Gene Transactivation, Metabolic Regulation, Chronotherapy, Cardiac Energetics.***

1.Introduction

The human body is both controlled by biology and by certain patterns of time that are built into its processes. Diurnal rhythms manage many body activities in a well-organized way, across short-term and long-term durations. Because it greatly affects health and disease, the circadian rhythm which follows a daily pattern has attracted much notice. When timings matter in medicine, it is known as chronopharmacology.

Specifically, chronopharmacology considers how taking medicine at certain times matched with the body's rhythms changes the therapeutic and side effects. Thanks to this new area of science, medication delivery can be timed with natural body processes to make drugs more effective and lower the chance of side effects. Even though researchers have been discovering the benefits of chronopharmacology for some time, this subject remains overlooked and poorly covered in many medicinal curricula everywhere(1).

Chronopharmacology began with observations made in the 19th century of repeated changes in the body's processes and drug effects. Nevertheless, it was in the early 1970s, thanks to Alain Reinberg and Franz Halberg, that modern concepts of racial biology began to appear. They showed that how the body responds to drugs and develops tolerance is related to the body's internal clock, making it important to time drug therapy properly. Afterward, studies have shown that rhythm influences the important steps in pharmacokinetics and how a receptor takes up and responds to drugs.

An important goal in chronopharmacology is to improve the benefits of taking medicine at certain times and to decrease the risks that come from taking it at the wrong times. As an example, the cycle of liver enzymes during the day influences what happens to certain drugs in the patient's blood and whether they are effective. Also, how much certain genes are expressed in cells can undergo changes, leading to differences in a drug's effects and risk of side effects. Noticing and using these changes in disease patterns can improve the accuracy and individualized approach to medicine.

Rhythms in the body are important in causing disease and the way symptoms develop, not just in how medicines act. A lot of common health problems, including heart, lung, digestive and cancer issues, have daily changes in terms of severity and how they develop. For example, heart attacks, strokes and severe asthma attacks are more likely at some times, so medication should be given at these times for best results. Because disease and bodily functions change throughout a day, using chronotherapy makes it possible to give medications when they will be most effective.

Silent application still poses several difficulties for chronopharmacology in medical care. Many healthcare workers, mainly medical students who will one day prescribe medicines, do not fully understand this field. A lot of medical learning programs have not yet integrated chronobiology and chronopharmacology into their syllabuses which may

stop medical experts from making correct decisions using timed medications(2).

Because of this lack of knowledge about biological timing, treatment may have poor results, bring on more harmful effects and cost more due to using more or less medication than needed. In addition, the rise of precision medicine means that chronopharmacology provides an inexpensive and highly personalized solution without the need for gene or diagnostic exams.

New developments in pharmaceuticals have helped make chronotherapy possible. Advancing systems for medicine delivery ensure that drugs are given at times matched with your body's daily patterns or the peaks and troughs of disease. They seem best suited for hypertension, asthma, peptic ulcer disease and specific cancers, where symptoms and drug effects vary a lot from day to day.

Recent studies show that clinical settings have profited greatly from chronopharmacological practices. Blood pressure control and the chances of cardiovascular problems can be better if people take their antihypertensive medications at bedtime. Giving inhaled corticosteroids just before bed is also useful for stopping asthma symptoms at night. Timing chemotherapy drugs such as oxaliplatin, to match people's daily cycles has improved their tolerance and has helped patients feel better.

As a result of these strong findings, we must assess how much medical students, who will become clinicians, know about chronopharmacology. If their knowledge is improved, they can better use this field to care for patients, support personalized medicine and achieve better health results. Also, students who learn about this field during undergraduate studies may be encouraged to study and develop new ideas in this sector.

This study was meant to find out how much medical students understand the role of chronopharmacology in medical practice. A well-structured questionnaire that requires knowledge of basic medical terms, when to administer each category of medication and the body's time-dependent reactions to drugs is helping the study identify where more learning is required. The result of this assessment will suggest possible solutions for enhancing the way chronopharmacology is taught in medical schools(3).

In essence, chronopharmacology is a progressive field that links how and when we give medicine to the natural rhythms in the human body. With the help of this discipline, healthcare can switch from treating everyone the same way to using precise and timed treatments that adapt to the body's patterns. It is very important that students in medicine have a solid foundation in these concepts for future effective care.

2.Methods

The purpose of this study was to determine how many and which undergraduate medical students in India are aware of and understand chronopharmacology. The investigators looked into students' comprehension of matters relating to drug timing, circadian impact and the medical significance of time-based drug use for diseases that have related rhythms.

Planning the Study and Caring About Ethics

It was decided to use a descriptive cross-sectional survey to see students' knowledge at a specific moment during medical education. It was chosen because it effectively quantifies how much of a given topic people in a population know, by using a set of organized questionnaires.

Before the study began, ethics approval was granted from the Institutional Ethics Committee of Sri Siddhartha Medical College, Tumkur. Having ethical approval meant the research followed accepted rules from around the world regarding participant rights, confidentiality and agreement to take part in the study. People were given all the information they needed about the study and were told that taking part was always their choice. Written consent was obtained from each participant which showed they agreed on a confidential and voluntary interview.

Which People Were Included in the Study

Students were selected at several medical colleges across India to make sure the sample reflected the variability of college environments and study materials. Research was done among students studying in the MBBS program across their entire period, from freshmen to those in clinical training.

Those who volunteered and gave their agreement were included in the study. There was no restriction related to gender, academic achievement or how much chronopharmacology students knew. Just those who went through the full set of questions were selected for the final analysis to have accurate and complete information(4).

Creation of the tool used to collect data

The depth and breadth of what participants knew about chronopharmacology was evaluated using a carefully crafted semi-structured questionnaire. An extensive review of relevant studies was done to design the questionnaire, so its questions refer to both what is known about biological rhythms and clinically important aspects.

Participation was organized into several parts that dealt with important areas.

This section focused on assessing the participants' knowledge of basic terms such as chronopharmacology, circadian rhythm, chronotherapy, etc.

This section reviewed circadian fluctuations in the GI system, paying attention to the best times for gastric acid secretion, changes in peptic ulcer symptoms and the most appropriate timing for H2 receptor blocker administration.

Participants' knowledge of when respiratory diseases, especially bronchial asthma, often occur was assessed. Experts explored questions related to when symptoms get worse, how well bronchodilators are working and the best time to use inhalational corticosteroids.

In this section, students gained knowledge of chronopharmacological approaches to cardiovascular disorders. I addressed concerns about the daily pattern of myocardial infarction, when antihypertensive drugs (ACE inhibitors and calcium channel blockers) should be given and the significance of fluctuations in blood pressure and heart rate due to body rhythms.

The final part of the course looked at the use of chronopharmacology in several cases, with attention given to the timing of oxaliplatin in bowel cancer therapy and the role of circadian rhythms in cholesterol processing and statin therapy.

There were multiple-choice questions in each section, with just one right choice for easy scoring purposes. Among a group of students, we pilot-tested the questionnaire to verify its clarity, usefulness and difficulty.

The Process for Collecting Data

Participant interviews took place throughout ten months, from the end of 2021 up until October 2022 to ensure as many as possible were included. We offered respondents the survey in paper or electronic form depending on each institution's capability and the students' preferences(5).

Students were given an explanation of what the study was about and why it matters to give correct answers. Students were expected to finish the questionnaire on their own without help from other resources to ensure their own ideas were shown.

Only the questionnaires with every answer provided were accepted for use in the analysis. Only fully completed and signed questionnaires were accepted so that the data would not be influenced.

The Handling and Study of Data

The data on the paper questionnaires were put into Microsoft Excel while electronic answers were gathered into a single database. All data was checked and adjusted to handle issues such as duplicate records and empty values.

It was set up to provide a numerical overview of participants' knowledge. The participants got one point for every correct answer and got zero if they chose incorrectly or weren't sure. We calculated each participant's total knowledge score by seeing how many questions they got right, out of the total number of questions.

To establish what was considered adequate knowledge, a participant needed 50% or more correct answers. Anyone with a score less than this target was deemed to have limited understanding of chronopharmacology. Classifying students as either proficient or not allowed simple identification of those who know enough and those who do not.

The data was summarized by performing descriptive statistical operations on frequencies, percentages and mean scores. To check for differences, the results were organized separately by year of study and gender. Looking at data from subgroups let us understand whether how much time was spent in medical school or in clinical practice shaped chronopharmacology awareness.

Because the fitness certification program was developed with a focus on description and discovering knowledge gaps, no inferential statistical testing was performed.

Shortcomings of the Research Study

Despite the fact that this study aimed to provide a thorough snapshot of students' chronopharmacology knowledge, some methodological problems require explanation. There is a chance that students may overstate their skills or give inaccurate answers from a questionnaire.

This study's cross-sectional approach does not allow us to establish causes of individuals' knowledge or changes in

knowledge over a period. The investigated group was limited to undergraduate medical students, so the knowledge of postgraduate trainees and practicing doctors was not included.

In addition, the survey didn't review all aspects of chronopharmacology, as it only focused on certain drugs and diseases affecting circadian rhythms. Conclusions may not work well in all cases due to the particular (geographic and educational) contexts and sampling strategies used.

Regardless of these issues, the findings pinpoint the existing state of knowledge about chronopharmacology among students and stress why additional support in this field is crucial.

3.Results

Altogether, 208 medical students from many medical colleges in India, in all years of undergraduate study and including interns, took part in the study. There was a good mix of MBBS students in the sample, with 38.5% in the third, 29.3% in the second and 24.0% in the first year. In addition, I heard from individuals in the fourth year (5.3%) and interns (2.9%). Of the students, 64.4% were female and 35.6% were male. Having these demographic details means we can assess training at various stages, thanks to the wide range of participants included in the study (Table 1).

Academic Year	Frequency	Percentage (%)
1st Year	50	24.0
2nd Year	61	29.3
3rd Year	80	38.5
4th Year	11	5.3
Intern	6	2.9
Gender		
Male	74	35.6
Female	134	64.4

TABLE 1 Demographic Distribution of Participants

The responses to the questionnaire were intended to judge knowledge of basic terminology and concepts of chronopharmacology and circadian rhythms for GIT, respiratory, cardiovascular and general disorders. People's answers showed that awareness of chronopharmacology is lower than their knowledge of its clinical applications.

The foundational knowledge explained the main ideas to 88% of participants, who then correctly said that chronopharmacology studies how drugs impact the body at different times. Moreover, 81.7% agreed that circadian rhythms are synchronized on a 24-hour cycle which suggests a good knowledge of chronobiology. Nevertheless, a small number of people linked circadian rhythms to segments of 6, 8 or 12 hours, showing that more accurate education on biological timing is important(6).

Despite showing positive results about common terms, information on the hands-on aspects of chronopharmacology was absent in many areas.

Gastrointestinal System

How gastric acid secretion and its clinical significance follow a daily pattern was not well understood by most students. Just 30.3% understood that gastric pH level is lowest and acid secretion is highest during the night, so it's important to take H2 blockers at night. In addition, about 70% of patients did not realize that their PUD symptoms get worse during the evening. I also found it notable that 76% struggled to pick the best time to use ranitidine by bedtime, so more acid could be reduced when there is most acid production.

Respiratory System

In bronchial asthma, it is usual for symptoms to increase at night or early in the morning. Even though it is widely known, only a little more than a third of people in the study said asthma attacks mainly happen at night. It was also found that just 20.2% of the participants understood that taking an inhaler with a corticosteroid at night helps it to work the best, since airway inflammation and narrowing both occur during nighttime. There were varied responses about when to take bronchodilator drugs, with most patients unclear about the best time for sustained-release medications to work best.

Cardiovascular System

There were even bigger know-how gaps in the field of cardiovascular chronopharmacology. A total of only 19.2% of students selected the early morning (6 am–12 pm) as the peak time for MI, though recognizing this is necessary since blood pressure and platelet aggregability differ between morning and evening. Only about a quarter (24.5%) of patients knew to take their ACE inhibitor enalapril at night and fewer than a quarter (23.1%) were aware that nifedipine should be taken in the morning. Because most doctors and patients are not aware of it, this suggests that the use of chronother1apy is not central to hypertension management education.

Miscellaneous Disorders

Concerns were raised about understanding both the proper time for chemotherapy and therapy to lower lipids. Giving oxaliplatin in colorectal cancer at 4 pm or a bit later, has led to fewer side effects and increased benefits for patients. But only a small number of participants, 22.1%, were aware of its importance which suggests most people lack depth of understanding in this field.

41.3% of respondents knew that our body produces the highest amount of cholesterol around midnight and 6 am in the morning. But 22.1% were unaware that taking statins at any time gives the same treatment results, showing that people are not fully sure about new studies recommending more versatile dosing(7).

Discussion of What We Don't Understand and the Implications

All this data demonstrates that there is a big gap between knowing basic chronopharmacology terms and knowing how to use them clinically. Many students knew that biological rhythms affect drug response, but most did not know exactly when specific disorders show signs or when drugs should be taken for best effect.

A lack of this knowledge may have clear consequences on patients. If we do not pay attention to biological timing in giving medications, they may not work well, cause more side effects and lead to unnecessary expenses. Since chronotherapy has helped manage hypertension, asthma, peptic ulcer disease and cancer treatment, the absence of student knowledge reveals the need to add more chronopharmacology to medical programs.

Tables Showing the Results

Scores for each question were organized into a frequency distribution that highlighted which subjects students knew and didn't know well. Chronopharmacology was correctly defined by 88% of students, while about a quarter of the students gave the right answer for timing ACE inhibitors and slightly less than a fifth for timing oxaliplatin.

4.Discussion

Because of the potential it offers to improve modern medicine, Chronopharmacology is quickly becoming well-known for studying how our bodies respond differently to drugs at different times. This research shows what medical students currently know about chronopharmacology and finds important areas where their learning fails to prepare them for applying these lessons in real-life medicine.

A number of internal rhythms in the body control diverse processes such as those in cells, organs and actions. They involve ultradian, circadian, infradian and circannual cycles, yet the circadian rhythm which lasts about 24 hours, is the most widely examined and applied for treatment. The key to this timing is a network made up of main and secondary clocks, all of which keep cells and organs synchronized to changes in light and dark(8).

Because of these circadian patterns, knowing how to time doses is important in chronopharmacology, as it affects both drug involvement in the body and its effects. Gastric acidity, liver enzymes, kidney function and receptor responses vary over a 24-hour period and affect how drugs are absorbed, travel, changed and excreted. Because fluctuations affect drug potency and problems, using specific times for drug administration is crucial.

Most medical students do know the basics of chronopharmacology and the body's 24-hour circadian rhythm, but they lack knowledge about how to use these concepts clinically. On the flip side, there is an understanding of theory, but it does not get put into practice in clinics.

Many students did not know that stomach acids increase during the night, an important cause of symptoms in peptic ulcer disease and why H2 receptor antagonists are taken at night. Gastric pH drops at night which doctors take advantage of by giving acid-suppressing medications just before sleep. Since the participants generally missed this factor, it is clear there are gaps in using chronopharmacology within pathophysiology.

Bronchial asthma also has clear changes in symptoms during the night and early morning. This increase at night is

thought to occur due to repeating changes in airway inflammation, bronchial hypersensitivity and activity of the autonomic nervous system. Data shows that inhaling corticosteroids in the evening leads to better lung health overnight and fewer symptoms upon waking. Nonetheless, a small number of participants were aware of this timing which underscores the need to further explain respiratory chronotherapy.

The heart and vascular system show strong daily changes, as blood pressure, heart rate and blood vessel tone change during the day. At the start of the early morning, when people's sympathetic activity and blood platelet aggregation are high, the risk of adverse heart events such as myocardial infarction and sudden cardiac death, also rises. Because blood pressure fluctuations happen daily, antihypertensive treatment should be timed to stabilize blood pressure and decrease cardiovascular risk. Still, the results show that not many students realize when ACE inhibitors and calcium channel blockers should be used which means their knowledge in this key area needs work.

The research points out that people often lack information about using chronotherapy for cancer chemotherapy. Oxaliplatin and other platinum-based drugs have features where giving them late in the day makes them less dangerous and easier to tolerate. Many medical students are not fully aware of it, perhaps mainly because chronotherapeutic approaches are complicated, not widely used and are not taught in depth in undergraduate years.

Also, even though cholesterol is made at the greatest level during the night, many students do not understand the reason for flexible statin use. The timing when statins are given has less impact on their benefits, because more recent evidence now calls for frequent updates in teaching(9).

Because of these frequent gaps in knowledge, several outcome issues arise. Lack of knowledge about chronopharmacology among medical students could bring about ineffective treatment and an increase in side effects with medications. This causes particular concern since chronic diseases such as hypertension, asthma and peptic ulcer disease place a heavy responsibility on the healthcare system and being prompt in management might greatly improve their results.

Secondly, if chronotherapeutic principles are ignored, it can lead to higher healthcare expenses, extra medication doses, more hospital visits for uncontrolled symptoms and greater side effects from drugs. Optimizing the time when medicines are given is a low-cost way to encourage patients to stick to their medicines, lower side effects and boost wellbeing, so chronopharmacology is advantageous where resources are scarce.

Similarly, because chronopharmacology is not taught in medical schools, it can discourage future efforts in the subject. Since there are quick developments in chronobiology and medical drugs, piquing the interest of medical students will help move chronotherapeutic strategies forward.

The way forward is to fully incorporate chronopharmacology into undergraduate medical training. Studies in this area could have specific subjects about biological clocks, problems related to them in health care and well-established methods for drug timing. Taking part in case studies, solving drug administration problems and practicing in clinical simulators may make knowledge about drug timing clearer and easier to remember.

As well as revising the curriculum, developing training workshops and courses for health professionals helps them stay up-to-date with the latest chronopharmacology concepts and use them in practice.

Latest drug delivery methods make it possible for medications to be released at the appropriate times according to a patient's biological cycle by using time-controlled release formulations and programmable pumps. Introducing students to these technologies will get them ready to make good use of them.

To conclude, collaboration among chronobiologists, pharmacologists, clinicians and educators encourages the creation of standardized chronotherapy processes for both teaching and clinical settings.

All in all, the study reveals that medical education lacks sufficient attention to applying chronopharmacology. Closing this gap through proper training is important for doctors-in-training to use biological timing to their patients' benefit. As precision medicine grows in healthcare, chronopharmacology provides a convenient method to support patient care by going along with their body's natural patterns.

5.Conclusion and Future work

Using biological time in medicine is giving rise to a revolutionary approach. By studying chronopharmacology, scientists can develop better, personalized and less harmful types of treatments. The findings show that medical students lack sufficient knowledge about chronopharmacology which might hold back the complete use of these principles in clinical practice.

Researchers found that while medical students understand the basics of circadian rhythms and chronopharmacology,

they still do not understand how it affects disease control and use of medication. Myocardial infarction, peptic ulcer disease, asthma, hypertension and cancer all needed clearer rules for when medications should be given, as this knowledge was not very common at that time. It appears that undergraduate medical courses pay little attention to chronopharmacology, meaning students are not ready to apply time-sensitive treatment approaches in practice.

As a result of this shortfall, many problems affect us. Failure to notice how treatment and symptoms change over the day can result in treatment that is less effective, more risky and causes the system to spend more money. On the opposite side, practices that organize when people take medicine to fit the body's rhythms increase the effectiveness of drugs, minimize possible negative effects and encourage patients to take their medications correctly. As a result, covering the educational gaps revealed here is necessary to fully use chronotherapy in healthcare.

To use chronopharmacology in medical education, experts must design a plan that uses more than one method. There should be dedicated courses or lessons in medical schools that address circadian biology, how medicines move through the body, respond to it and chronotherapy protocols. Helpful practice activities and clinical scenarios using chronotherapeutic topics may boost students' knowledge and learning skills.

It is important for curriculum makers to make sure that the latest research and proofs in chronopharmacology are integrated into the curriculum regularly. As improvements in pharmaceuticals come, with systems that can deliver certain amounts of drugs and chemotherapy timed for maximum benefit, students must know about them to use them properly.

Even after undergraduate education, continuing medical education with workshops is important for practicing doctors to learn the latest in chronotherapy. If studies guide clinical actions, healthcare will make biological timing a key point in treatment choices.

If healthcare policymakers and regulators understand chronopharmacology, they can better develop plans and policies that lead to more time-content drug regimens. Through such programs, pharmaceutical companies may have more reason to launch medicines and tools that follow a chronotherapy schedule, bringing them into use more quickly.

Also, further study on chronopharmacology should be done for many diseases and types of drugs to guide better treatment decisions. By combining efforts, chronobiologists, pharmacologists, clinicians and educators will be able to carry out research findings into common applications and teaching materials.

Cost-saving is one of the main advantages of using chronotherapy. Getting drugs to patients at the right time can reduce drug requirements, lower risks of adverse reactions and cut hospital admissions, both saving money for healthcare institutions and for patients. Efficient use of treatments is extremely important when resources are limited.

Overall, chronopharmacology is at the forefront of the progress in personalized medicine. Matching the timing of drugs to the body's natural rhythms helps treatments work well, reduces potential harm and makes them easier for the patient to take. The findings emphasize that educating medical students is important for the following generation of doctors to feel more confident treating diseases using chronotherapeutic approaches.

Incorporating chronopharmacology into both teaching and practice can enhance patient care, hold down costs and encourage progress in the field of pharmacotherapy. Greater knowledge about when biological processes happen and more advanced technology will likely make chronotherapy a major part of precision medicine.

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The authors have no conflicts of interest to declare

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