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Original Article

Estimation of the Knowledge of Some Libyan Pharmacists About Chronopharmacology of Antihypertensive Medications

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ABSTRACT

Aims. *The present study aimed to investigate the knowledge of Libyan pharmacists about the concept of chronopharmacology of antihypertensive medications.* ***Methods.*** *Questioners were studied at the East region (Cities) of Libya (Albyda, Benghazi and Almarj). All the samples were analysed by Excel Software. The pharmacists were asked to fill the questioner whether the antihypertensive medications are given in the morning, evening, bed time, anytime or not sure.* ***Results.*** *Although they did not know about the concept of chronopharmacology, findings shows that 50% of the of the pharmacists in the current study described the tested medications to be taken on the right time dependent on the type of each one.* ***Conclusion.*** *The current study indicated that the practice of pharmacists regarding to the awareness of chronopharmacology concept needs further improvement. The improvement can be done by contribution of healthcare professional and providers to feedback about the importance of chronopharmacology.*

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INTRODUCTION

Chronopharmacology is a branch of chronobiology which is the study of biological rhythms. This subdivision deals with differences in the pharmacological effects of a drug in regard to the chronological variation in biological functions and endogenous systems at regular intervals [1-3]. The human body shows distinguish changes in biological functions during 24 hours, known as circadian rhythm based upon the sleep activity cycle. In some individuals, the inherited period of circadian rhythmicity is not exactly 24 hours, while in other individuals it may be longer than 24 hours [4]. Pathological changes alter this circadian-rhythmic behavior from normal to abnormal. All bodily functions are under the influence of internal factors such as genes, the autonomic nervous system, vasoactive hormones, and hematological and renal variables [5]. Circadian-rhythmic and dosing timetables influence the efficacy and toxicity of a number of drugs by biochemical, behavioral, and physiological means. Some drugs cause changes in 24-hour rhythmic cycles and cause alterations in hemostatic status that are apparent as a disease. Changes in 24-hour rhythmicity are fundamental in the adverse effects of a given drug [6]. Differences in the timing of drug administration alter the therapeutic outcome of anti-inflammatory, antiasthmatic, chemotherapeutic, cardiovascular, and antiulcer therapies among others. The success of chronopharmacology is based on maintaining a drug level in the blood within the therapeutic range, mainly during the period of disease severity [7].

The pattern of blood pressure and heart rate differs between hypertensive and normotensive people [2]. The Sympathetic outflow is greater among hypertensive and normotensive individuals early in the morning (4:00-6:00 am) than during the rest of the day. The level of sympathetic activity decreases during sleep time [8]. Systolic blood pressure increases rapidly by 20–25 mmHg, and diastolic blood pressure increases by 10–15 mmHg upon awakening. Commonly there is a nocturnal decrease in blood pressure both in normotensive and primary hypertension. Blood pressure starts rising during the initial

period of the day and reaches its maximum at around 10 am. However, a gradual fall in blood pressure starts around 7:00 pm in the evening, and a maximum fall is observed between 2:00 and 5:00 am in the morning [2, 8].

Hypertension affects the vast majority of the Libyan population including both genders; males and females. Numerous factors participate in the incidence of this disease such as age, obesity, hereditary, lifestyle, and cardiovascular system abnormalities. Blood pressure, heart rate, peripheral resistance, and the release of vasodilation neurotransmitters all display pronounced circadian rhythm variations. Circadian rhythm plays a crucial role in the regulation of blood pressure levels in the human body throughout the day and night cycle. Therefore, any changes in the normal circadian rhythmic pattern of blood pressure led to development. The goal of chronopharmacology is to determine the most suitable time for the administration of a drug to enhance efficacy and safety, prevent tolerance, and minimize the unwanted effects of the given therapy. This can be achieved by specific drug technologies but often by simply adjusting the time of the administration of conventional therapy. Based on the concept of chronopharmacology; drugs ingestion time and drug effectiveness are extremely connected to the biological clock (circadian rhythm) in the human body. Regarding the topic in the present study; well-e educated medical professionals such as pharmacists will be able to guide the patient to take his or her medicines the right way. However, a lack of information about chronopharmacology and the role of circadian rhythm in biological functions regulation leads the pharmacists to choose random time of drug administration. As a result, this could make the treatment totally ineffective. The importance of the present research came from giving the antihypertensive therapies in the precise time based on the pharmacist's knowledge about the concept of chronopharmacology.

METHODS

Research question

Does Libyan pharmacists from the East region have an awareness about the concept of chronopharmacology of antihypertensive medications? The questionnaire including the most common used antihypertensive medications such as Calcium Channel Blockers (CCBs), Beta-Adrenoceptor Blockers, Angiotensin II receptor blockers (ARBs), Alpha-Adrenoceptor Blockers and Angiotensin-converting enzyme inhibitors (ACEs).

Data collection procedure

This study was a descriptive cross-sectional study, using a questionnaire to collect data from several pharmacies at the major cities located in the eastern region of Libya. The targeted cities were Albyda, Almarj and Benghazi. Over 600 questionnaires were distributed on the pharmacies at these cities. Questioners left at the pharmacies for few days to give the pharmacists enough time to be completed. Based on the questionnaire, pharmacists asked to choose whether the antihypertensive drugs targeted in this study taken morning, evening, bed time, anytime and not sure. After that all questionnaires were collected from the pharmacies and underwent to statistical analysis by Excel software. Unfortunately, many pharmacists refused to complete filling the questionnaire, thus from 600 only 411 questionnaires were completed.

RESULTS

In the current work, about 42% agreed to give the ACEs in the morning (Figure 1). While 22% of the pharmacists chose the evening time for ACEs to be taken (Figure 1). However, 12% were not sure which time to choose. Another 12% said that the patients could take their ACEs at any time or at bedtime respectively (Figure 1).

About 50% of the pharmacists chose to give CCBs in the morning, whereas, 17% said the evening was better to give the patient this kind of medicine. On the other hand, CCBs were chosen to be given anytime from 13% of the tested pharmacists. The lowest percentage, 10% was evenly chosen for bedtime or not sure (Figure 2). The highest percentage of the pharmacists (40%) agreed to give βBs in the morning while 17% were confident to give βBs at bedtime. However, taken βBs in the evening were chosen by 16% of the pharmacists used in this study. 15% and 12% agreed to give βBs at any time or were not sure respectively (Figure 3).

Findings in the present study show that 36%, 18%, and 16% of the pharmacists choose to give ARBs in the morning, at bedtime, and at any time respectively. However, 15% of them were not sure and 15% selected evening time (Figure 4). The morning time (34%) represents the highest percentage in the αBs group. However, evening time was chosen only by 17% of the sample. while 18% were not sure, 16% and 15% choose to give αBs at bedtime and at any time respectively (Figure 5).

In summary, data shows that the highest percentage of the tested pharmacists chose the morning to be the best time for the patients to consume their medications. Parentages were as following, CCBs (50%), βBs (40%), ARBs (36%), αBs (34%) and ACEs (42%). Whereas, the second-highest numbers were chosen for evening time 17% and 22% for CCBs and ACEs respectively.

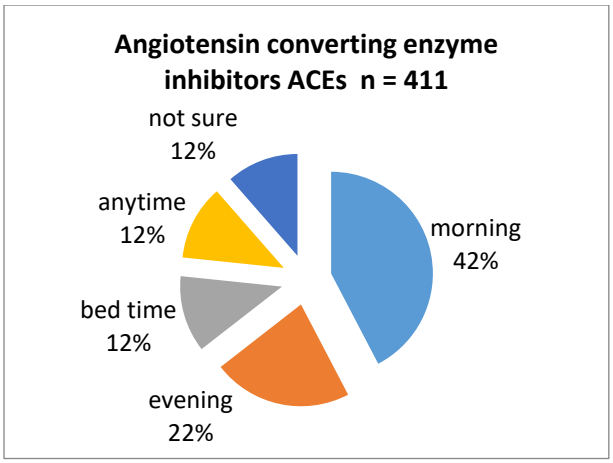

Figure 1. 42% of our sample agreed to give Angiotensin-converting enzyme inhibitors ACEs in the morning time while 22% and 12% preferred to give this treatment in the evening or at any time respectively. 12% said at bed time and 12% of the pharmacists were not sure.

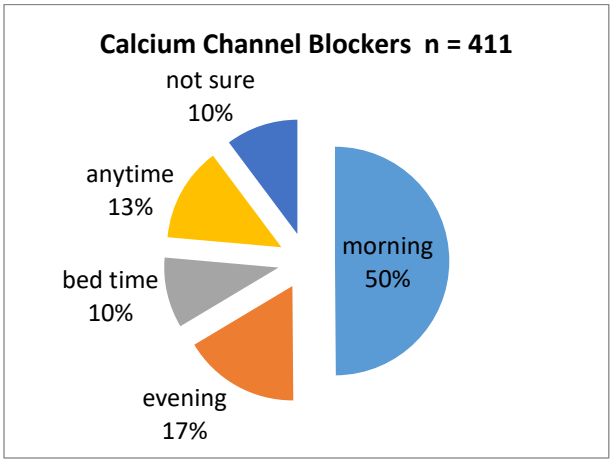

Figure 2. 50 % of our sample agreed to give calcium channel blocker in the morning, while 17% and 13% chosen to give this treatment in the evening or at any time respectively. 10% said at bed time and 10% of the pharmacists were not sure.

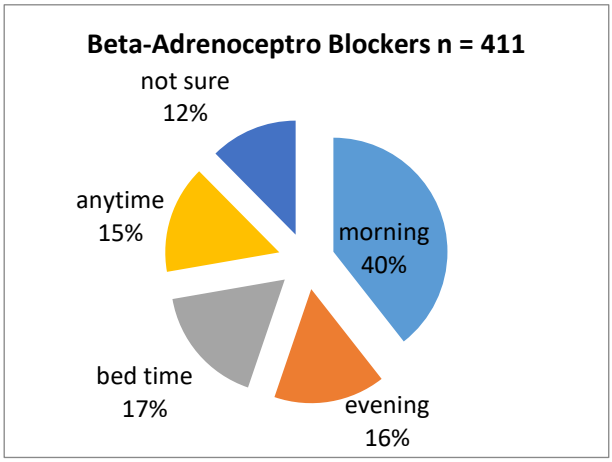

Figure 3. 40% of our sample agreed to give beta blocker in the morning time while 16% and 15% preferred to give this treatment in the evening or at any time respectively. 17% said at bed time and 12% of the pharmacists were not sure.

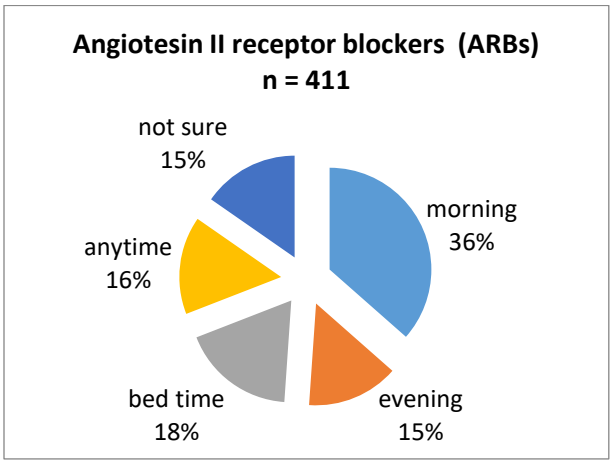

Figure 4. 36% of our sample agreed to give Angiotesin II receptor blockers in the morning time while 15% and 16% preferred to give this treatment in the evening or at any time respectively. 18% said at bed time and 15% of the pharmacists were not sure.

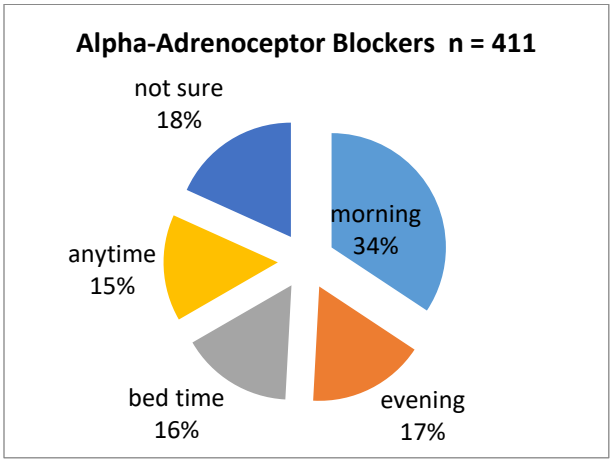

Figure 5. 34% of our sample agreed to give Alpha-Adrenoceptor Blockers in the morning time while 17% and 15% preferred to give this treatment in the evening or at any time respectively. 16% said at bed time and 18% of the pharmacists were not sure.

DISCUSSION

It has been suggested that loss of the physiological circadian pattern of blood pressure may lead to a pathological mechanism associated with increased morbidity and mortality [9]. Chronically increased BP may even lead to general dysfunctional circadian body rhythms. For all blood pressure profiles with impaired, disturbed, or otherwise deviating rhythmicity compared with a normal diurnal pattern, it was confirmed that there is a clear association with the risk of cardiovascular disease [9]. Normalization of the circadian rhythm of BP is one of the primary targets in the treatment of hypertension. The vast majority of reviews have shown normalization of the dipping profile and/or changes in asleep BP values when applying chronotherapy, and this fact may have even more clinical impact than the differences in the mean 24-h BP reduction alone. Several studies have been performed with all available classes of drugs used in the treatment of hypertension, such as, ACE inhibitors, α-blockers, β-blockers, direct renin inhibitor, angiotensin receptor blockers, and calcium channel blockers. Significant treatment-time differences were confirmed for several classes of antihypertensive drugs. Most researches have shown that the majority of patients with hypertension take their medicine in the morning; some data showed up to 80% of patients with hypertension taking all antihypertensive drugs in the morning. In addition, β-blockers appeared to be more effective in morning administration. It is also distinguished that CCBs are recommended to be given in the morning by several studies. Administration of sustained-released verapamil or diltiazem in the morning showed effective control over 24-hour blood pressure profiles [10,11].

In addition, chronic administration of ACEs (enalapril) in the morning significantly decreased blood pressure during the day [12]. Hermida et al. evaluated the influence of ingestion time on the efficacy of spirapril to essential hypertensive patients in the morning showed a significant reduction in the ratio of blood pressure [7]. However, a quite recent studies have focused on drugs acting and have indeed shown more drug's efficacy when antihypertensive drugs were given in the evening [12, 13]. Thiazide diuretics shows a greater efficacy with evening treatment, being significantly more effective in reducing the incidence of severe cardiovascular events [14, 15]. Data from more than 2,000 patients with primary hypertension were compared by meta- analysis study and established that more efficient BP control was achieved when the antihypertensive agents were giving in the evening [16].

Pharmacist's knowledge about morning versus evening administration of antihypertensive medications shows consistent variations for majority of our samples. CCBs were selected by 50% of the pharmacists to be taken in the morning. This was a strong indication that the pharmacists in the current study have at least the basics knowledge how to describe this group of medicines in the right time. In addition, the highest percentage (42%) of the samples in the present work, decided to give the ACEs in the morning. This shows that some of the pharmacists in this project have the experience about the right ingestion time of the ACEs inhibitors. However, 22% of the sample preferred the evening time for ACEs. In the same context, 17% of the sample select to give CCBs in the evening time.

Finally, all studies in this research showed that most of antihypertensive drugs used today could be taken either in the morning or in the evening time during the day. The highest percentages of our study suggested that the pharmacists recommended the antihypertensive patients to consume their medicines in the morning CCBs 50%, ACEs 42%, βBs 40%, ARBs 36% and αBs 34% or in the evening time CCBs 17% and ACEs 22%. Unfortunately, about 50% of the examined pharmacists in this study have no idea about the concept of chronopharmacology and chronotherapy of Bp-lowering drugs. Therefore, pharmacists should be encouraged to enhance their background and further studies about chronopharmacology and chronotherapy should be carried out.

CONCLUSION

Pharmacist's knowledge about chronopharmacology and circadian rhythm variations play a significant role in anti-hypertensive therapy. Chronopharmacology and chronotherapy formed a vital factor for most of the medications used for chronic diseases nowadays. Chronotherapy of antihypertensive drugs should be employed to achieve better optimization of therapeutic with fewer adverse effects. Chronotherapy of different antihypertensive classes should be studied and discussed in more detail to make it a beneficial and implementable area of clinical practice.

Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

Conflict of interest

There are no financial, personal, or professional conflicts of interest to declare.

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