ABSTRACT

Objective: To assess the pharmacists’ perception and knowledge regarding the use of some chronic medication and appropriate administration timing.

Methods: A cross-sectional survey was developed and randomly distributed to local retail pharmacies in the western region of Saudi Arabia between February 2019 to May 2019. We randomly selected 500 pharmacists at different shifts.

Results: The response was 86% of the sample we have selected. 90.7% responded that patients’ daily routine plays a major role in their disease status such as diabetes, hypertension, and hypercholesterolemia. More than 76.3% of respondents did not know that blood pressure peaks in the mid-morning and in the evening but goes lower early in the morning. Only 40.9% knew that calcium channel blockers will be more effective if given in the late evening than in the morning.

Conclusion: The findings here suggest that more training, education and/or workshops will be beneficial in understanding medication time to produce an optimal effect.

Keywords: Pharmacists; pharmacology; chronopharmacology; drugs; hypertension.
1. INTRODUCTION

Medication administration timing “chronopharmacology” looks after normal human biological processes and medications’ effects after various times during the day [1]. The normal processes in the human body follow certain biological rhythms and that have shown to affect physiology and pathophysiology of several medical conditions as well as various medications effects and side effects [1-3].

Among the cardiovascular disease is hypertension that is known to affect over 20% or locals with more males than females. It is a widespread disease that is on the rise according to local officials [4,5]. The various fluctuation in blood pressure is due to the continuous synchronization of the cardiovascular system including heart rate (HR), peripheral resistance, as well as circulating vasodilation hormones with their profound effects.

Blood pressure and HR are in continuous variation throughout the day [1,6]. In this case, drugs that affect this rhythm will need to take into consideration the appropriate timing to produce optimal effects. Because vascular resistance and cardiac outputs are changing continuously as aforementioned due to physical and physiological variation (angiotensin, renin, aldosterone, epinephrine, norepinephrine, etc) day and night in addition to environmental factors. Administering related drugs will have variations in their effects according to the time of administration [2,6-8].

Blood pressure lowering chemical agents (angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), calcium-channel blockers [CCBs], α-blockers, β-blockers, and diuretics) will produce a certain effect at a certain time according to biological rhythms [9]. The magnitude of their effect and the variation throughout the day was illustrated by other researchers.

Clinically significant differences in blood pressure between morning and evening dosing of antihypertensives single or combination therapy of angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), calcium-channel blockers [CCBs], α-blockers, β-blockers and diuretics was demonstrated in several studies. The issue is with patients not knowing such variations and not able to synchronize with it while administering their therapy [8,10].

In recent years, we noticed that the role of pharmacists either hospital-based or community based has developed greatly, especially with the integration of patient-oriented healthcare systems away from the traditional role of the pharmacist as the agent responsible for dispensing medications only. The patient-oriented healthcare system aims toward improving pharmaceutical outcomes, reducing adverse drug reactions, minimizing or prevent drug interactions, reducing hospital stay, and the overall cost of care [11-13].

We have selected hypertension for various reasons. Among which, is the prevalence of the disease locally and worldwide. The condition occurs when blood pressure exceeds 130/80 mmHg according to the American College of Cardiology [14,15]. High blood pressure affects people of different ethnic backgrounds, races, social, and economic status. The disease usually associates with certain risk factors including family history, kidney disease, diabetes, or other metabolic syndrome conditions [14,16].

Hypertension if left untreated or under-treated will lead to serious complications that eventually cause death [8,16]. Many male patients, specifically, will become hypertensive by the age of 50 [4,14] several studies looked into hypertension management and reported that up to 70% of treated patients are under-treated. In our region, medication compliance is a serious matter, and especially with hypertension medications [17,18].

We here tried to assess the current practices and knowledge of all retail pharmacists who were selected to conduct this survey on their understanding of medication chronopharmacology, specifically high blood pressure therapy through a cross-sectional questionnaire-based study focusing mainly on patient counseling practices at retail pharmacies in the selected region and how impactful is that on patients’ adherence to medication dosing timing according to biological rhythm? We also looked into pharmacists’ perception and knowledge of several antihypertensive medications and their routine while providing patients-oriented care “patient’s counseling”.
2. METHODS

A cross-sectional questionnaire was surveyed utilizing both quantitative and qualitative approaches. It consists of closed and open-ended questions for respondents to answer. The sample size was 430 retail pharmacists in the western region of Saudi Arabia. All subjects were randomly selected and surveyed to answer all questions. An electronic form was created utilizing a “Survey Legend” online survey tool. The link was sent to all randomly selected pharmacists who agreed to participate. Pharmacists were 72% males and 28% females. Neither human nor animal subjects were involved in this study.

Analysis of all responses was carried out using the statistical package SPSS for Windows version 24.0 (SPSS Inc., Chicago, IL, USA).

3. RESULTS

The participants’ response was 86% of the surveyed pharmacists. Most (90.7%) were in favor of the direct effect on blood pressure by the level of physical activity, emotional, environmental factors, and endocrinological fluctuation. On the other hand, 47.7% of surveyed pharmacists were not aware of blood pressure highs and lows throughout the day, Fig. 1.

In response to questions related to knowledge assessment of chronopharmacology of antihypertensive drugs. Regarding diuretics use for better effect and convenience, 74% of subjects confirmed early morning administration (Fig. 2). With regards to calcium channel class of medication (nifedipine), 41.2% of participants were aware of the appropriate timing to be late in the evening for better blood pressure lowering effect.

The surveyed pharmacists acknowledged the importance of providing additional drug use information while counseling them was (91.2%). Counseling pharmacists must touch base with patients on drug frequency (93%), time of administration AM or PM (28%), supplementing patients with readable information (91.2%), drug-administration time relationship for the desired outcome (67.7%). The importance of patients’ level of education, culture and environmental factors while providing counseling came to be (69.3%). Patients’ preference with regards to when to administer medications was favored by 46.7% of participants Fig. 3.

4. DISCUSSION

Our findings showed a considerable level of retail pharmacists' knowledge and appreciation for various drug dosing and its relationship to optimal effects and its importance to be delivered to patients while dispensing hypotensive drugs. 15% of pharmacists insisted on providing all related dosing time to patients as being extremely important. On the other hand, 43% think they provide such information since it is not of great importance during patients' counseling.

We noticed that participants’ responses to questions related to their knowledge on normal human biological rhythms and processes that affect blood pressure causing the daily peaks and troughs, the responses reflected poor knowledge as shown in Figs. 2 and 3. 44.7% of collected responses disagree with better morning dosing of angiotensin converting enzymes inhibitor (ACE-I) (e.g lisinopril, quinapril) and angiotensin receptor blockers (ARB) (e.g. losartan, candesartan). And 43.5% of responses showed disagreement with evening dosing of calcium channel blocker (CCB), ACE-I and ARB to improve the blood lowering effect. This consists with our finding of 47.7% of participants not aware of the morning and evening normal peaks of blood pressure.

The patient’s preference for when to take his/her medications was favored by 46.7% of our sample. Even though, the majority of participants (82.3%) agree on the need to take medications according to the best time considering the normal human biological rhythm for morning and evening dosing.

It is an established knowledge and confirmed by trials that patients’ response to hypotensive therapy will be better achieved by changing dosing time rather than combining several bills at the same time. Such practice of combined bills showed more side effects than overall control of the condition [9,19]. In one study in non-dipper patients suffering from advanced kidney disease, expressed lower nocturnal blood pressure levels just by moving hypotensive therapy administration time [20].
How the influence of hypotensives drugs on blood pressure is still a matter of debate.

Some medications when given at certain time produce good therapeutic effects, but it produce sub therapeutic effect in other time

Blood pressure has two peaks (9 AM and 7 PM), trough around 3 AM

A different effect on blood pressure values depends on the time of medication administration

Physical activity, stress, enviromental, and endorine alterations affects daily blood pressure

Fig. 1. Knowledge of biological rhythms of hypertension (n=430)

PM dosing of an ACE-I, ARB is more effective as a hypotensive than AM dosing

AM dosing of a diuretic/ACE-I combination is more effective in hypotensive effect than AM

PM dosing of CCB/GTN is more effective than AM dosing

CCB/ARB combination optiaml efficacy as hypotensive is not related to time of administration

PM dosing of a CCB as a hypotensive is better than AM dosing

PM dosing of an alpha B shows optimal effect than early AM dosing

AM dosing of a BB is better than PM dosing

Fig. 2. Knowledge of chronopharmacology of antihypertensive medications (n=430)
5. CONCLUSION

Our findings suggest further workshops and training to implement a patient's counseling program and longer patient-pharmacist contact time for better health outcomes. Pharmacists' knowledge of hypotensive drugs administration time is at an acceptable level but rarely delivered to patients. Chronopharmacology is extremely important for various chronic diseases management and so should be integrated into overall pharmaceutical care at the point of contact.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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