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ANTIHYPERTENSIVE MEDICATIONS AND CHRONOPHARMACOLOGY: ROLE OF SAUDI PHARMACISTS IN PATIENT EDUCATION

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ABSTRACT

***Objective*:** This study aims to evaluate the practice and knowledge of Saudi pharmacists regarding chronopharmacology of antihypertensive drugs.
***Method*:** A Descriptive cross – sectional questionnaire based survey of randomly selected community pharmacists from Riyadh city in Kingdom of Saudi Arabia in March and April 2014. Sample consisted of randomly selected 100 community pharmacists.
***Results*:** 100% of participants agreed that physical activity, stress, environmental, and endocrine alterations affect daily blood pressure. However, 35% did not know that blood pressure has two peaks; around 9:00 am and 7:00 pm, and one drop around 3:00 am. In addition, 24% of pharmacists did not know whether or not evening dose of nifedipine and GTN was more successful in decreasing the blood pressure as compared to the early hours in the morning.
Conclusion: Our study shows that knowledge and practice of community pharmacists need further improvement about interaction between time of administration of anti-hypertensive drugs and its efficacy.

INTRODUCTION

Chronopharmacology is the science that investigates the biological rhythm dependencies of medications (Ohdo, 2010). Biological rhythms were shown to impact the physiology and pathophysiology of diseases, as well as the efficacy and toxicity of many drugs (Ohdo, 2010; Farrow *et al*., 2012; Ohdo, 2010; Koppisetti1 *et al*., 2012 and Liu *et al*., 2011). Hypertension affects about 15.1% of Saudi population including 17.7% males and 12.5% females and these percentages growing with age, according to Saudi ministry of health statistics in 2012 (http://www.moh.gov.sa/en/Ministry/Statistics/book/Documents/1433.pdf). The cardiovascular system is highly organized in time; blood pressure (BP), heart rate (HR), peripheral resistance, the release and activity of vasodilating hormones with pronounced circadian variations. Cardiovascular functions such as heart rate and blood pressure show 24 hour variation, so administering of antihypertensive medications to patients should be time dependent in order to give maximum blood pressure control regarding chronopharmacology. Blood pressure is known to show a 24-hour variations as a result of different factors, such as, cyclic day–night alterations, rest–activity alterations, behavioral changes (such, diet, meal timings, and mental stress), environmental factors (including temperature and noise levels) and physiological circadian rhythms, such as plasma noradrenaline and adrenaline levels, and renin, angiotensin and aldosterone levels (Farrow *et al*., 2012; Ohdo, 2010; Sukumaran *et al*., 2010 and Hermida *et al*., 2013).

The efficacy of antihypertensive agents was determined when given at right time according to biological rhythm (Koppisetti1 *et al*., 2012). Clinically significant differences in blood pressure between morning and evening dosing of antihypertensive 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. However, majority of hypertensive patients are unaware and not adherent to biological rhythm when taking their antihypertensive medications (Hermida *et al*., 2013 and Salles *et al*., 2008). The role of pharmacists has evolved from being "product oriented" focusing on dispensing

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of medications to "patient-oriented" focusing on patient education and provision of pharmaceutical care, leading to decreasing Drug-related morbidity and mortality, and reducing the number of adverse drug reactions (ADRs), the length of hospital stays, and the cost of care1 (Makowski *et al*., 2013 and http://www.who.int/mediacentre/news/releases/2012/world_health_statistics_2012-0516/en/). This cross sectional survey-based study aims to evaluate the practice and knowledge of Saudi pharmacists regarding chronopharmacology of antihypertensive drugs. To our best knowledge there are no previously published reports assessing the knowledge and practice of Saudi pharmacists regarding chronopharmacology.

Hypertension

Hypertension is basically a raised diastolic or systolic blood pressure more than or equal to 140/90 mmHg as mentioned by the World Health Organization (W.H.O). This condition is now an important health issue in both developed as well as developing nations. Factors of risks linked with the growth of hypertension are improved by intake of alcohol, obesity and overweight, poor diet (particularly, salty food), shortage of physical exercise, gender, advanced age and family history (Hermida *et al*., 2013 and El Bcheraoui *et al*., 2014). The importance of high blood pressure as a major cause of common serious diseases and deaths has been recognized in most countries particularly Western countries (Persell, 2011). Hypertension affects more than a quarter of the global adult population including Kingdom of Saudi Arabia (KSA). It is projected in year 2025 to increase by 24% in developed countries and 80% in developing countries (El Bcheraoui et al., 2014). Hypertensive Patients in Saudi Arabia having decreased adherence to their anti-hypertensive treatments. In trying to realize the reasons behind decreased adherence, research in Saudi Arabia has emphasized on just one factor. Holistically dealing with all the linked factors, i.e., those linked with providers, health system, and patients, would thus be an important step for improving behavior of adherence among Saudi patients having hypertension problem (Wright *et al*., 2010).

Antihypertensive Medications

Patients who face primary hypertension are normally handled with medications which:

- Decrease the volume of blood (that decreases cardiac output and central venous pressure)
- Decrease systemic vascular resistance
- Decrease the cardiac output by depressing stroke volume and heart rate

Patients who face secondary hypertension are normally handled by removing or controlling the primary pathology or disease, however they can still need anti-hypertensive medications. Anti-hypertensive drugs are a category of medications which are consumed for treating hypertension (high blood pressure) and also to avoid the problems of high blood pressure, like myocardial infarction and stroke. Proof recommends that decrease in blood pressure by 5 mmHg may reduce the danger of stroke by 34%, of ischemic heart diseases by 20% and decrease the possibility of heart failure, dementia and death from heart disease. There are multiple categories of anti-hypertensive that reduce the blood pressure by separate means; among the most significant and most commonly consumed are the A.R.Bs or angiotensin II receptor antagonists, beta blockers, calcium channel blockers, A.C.E inhibitors and thiazide diuretics (AlGhurair *et al*., 2012). Patients with hypertension have not proper general awareness and knowledge regarding hypertension. They didn't identify the significance of blood pressure (S.B.P) control and didn't worry regarding measurement of normal blood pressure (B.P). Thus, research shows that in fifty to seventy five percent of diagnosed hypertensive patients, their hypertension condition isn't controlled, and is still a major issue in the developing nations. On other hand, patients with this condition think that this illness is not considerable and serious, and hypertensive medications have multiple side effects therefore they should just use it when they think that symptoms of high blood pressure like dizziness, chest pain, headache or following blood pressure monitoring (White, 1996). Thus, all attempts are made to enhance the practice, attitude, awareness, and knowledge of patients with this condition, particularly regarding the dangers linked with un-controlled hypertension, and to design control and preventive programs about this problem.

Research Question

The research question for our investigation is stated as "Does patient counseling provided by Saudi pharmacists have a positive impact on medication adherence to biological rhythm?"

Research Objectives

1. To measure pharmacists knowledge about chronopharmacology of antihypertensive medications
2. To assess pharmacist's practice when providing patient counseling for hypertensive drugs.

METHODS

This is a descriptive research, where cross-sectional survey was conducted. This research made use of both quantitatibe and qualitative research design, where researcher-led questionnaire has been utilized to carry out this research. The questionnaire consists of closed and open-ended questions. Our sample consisted of randomly selected 100 community pharmacists from Riyadh city in Saudi Arabia. The majority of pharmacists, 87 pharmacists (87%) held a bachelor degree in pharmacy and nearly half of them, 54 pharmacists (54%) have an experience working in the pharmacy profession ranging from 6 to 10 years. There was no ethtical approval required since no human/animal subjects were used. Special care was taken in order to maintain confidentiality by coding questionnaires after data collection. Data was analyzed utilizing descriptive statistics making use of Microsoft Office Excel 2010 to provide an overview of the quantitative data that has been collected through survey.

RESULTS AND DISCUSSION

As shown in Figure 1, all of our study participants (100%) agreed that physical activity, stress, environmental factors, and endocrine alterations affect daily blood pressure. However,

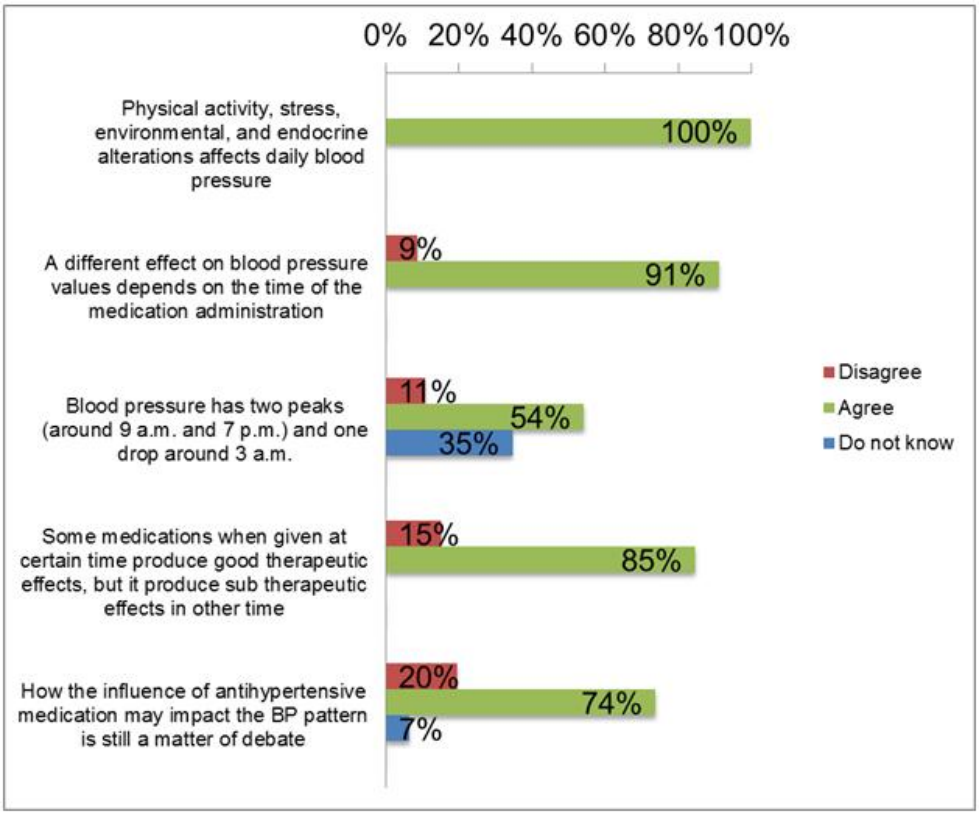

Figure 1. Awareness of Saudi pharmacist about Biological Rhythms of Hypertension (n=100)

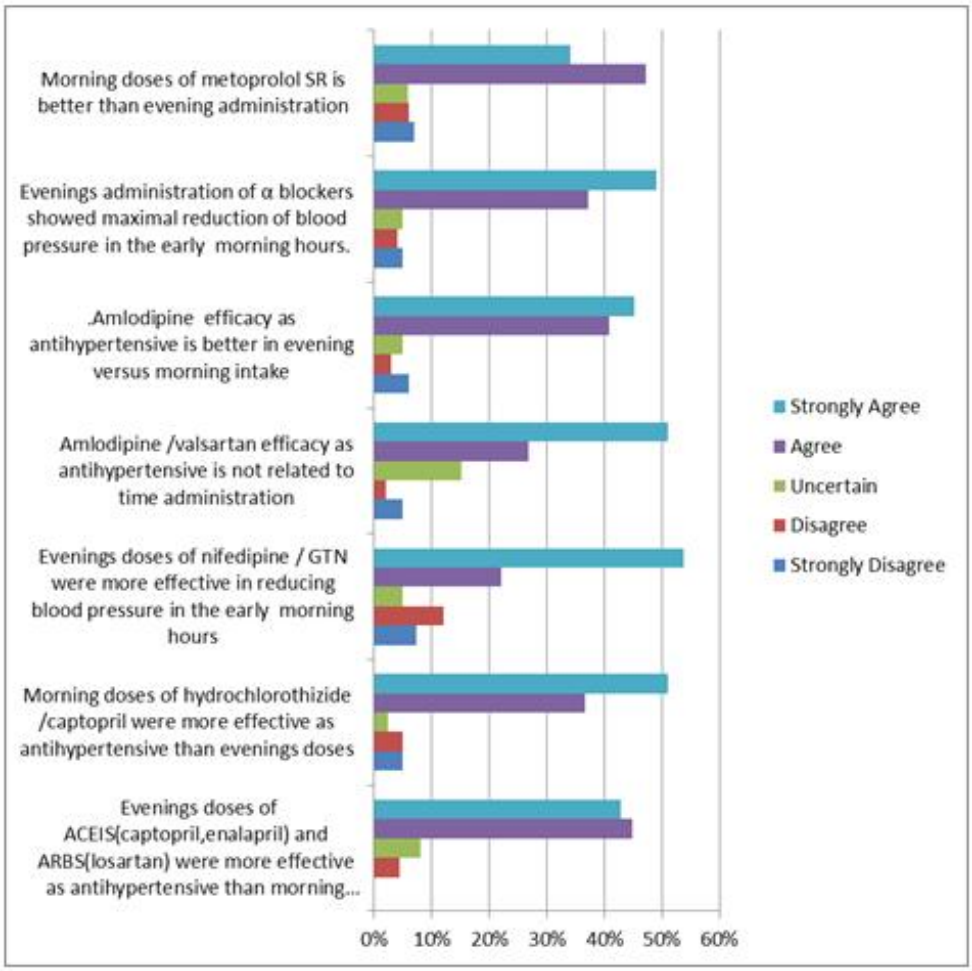

Figure 2. Awareness of Saudi pharmacist about chronopharmacology of antihypertensive medications (n=100)

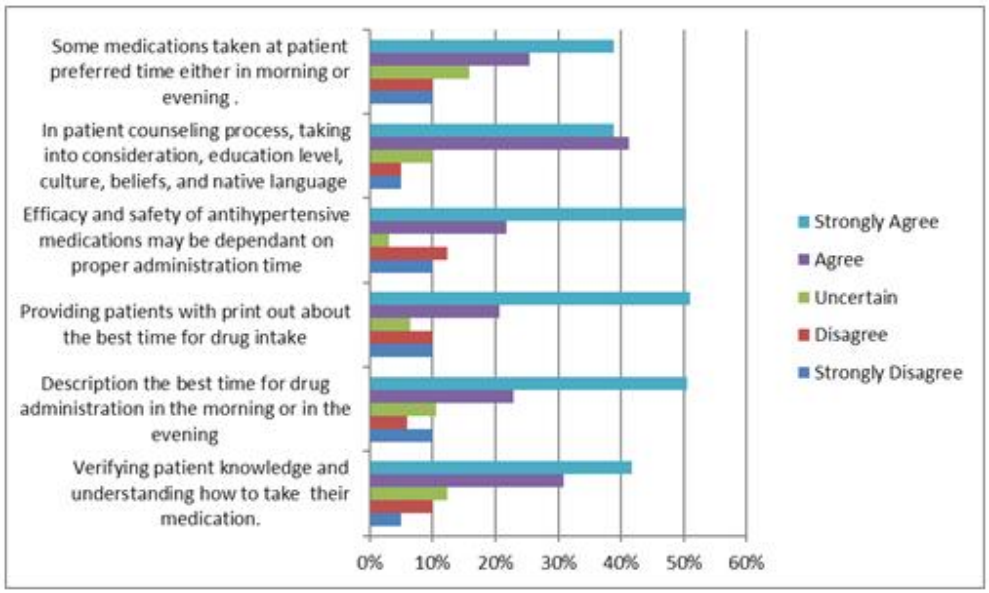

Figure 3. Contribution of pharmacist counselling hypertensive patient (n=100)

35% did not know that blood pressure has two peaks; around 9:00 am and 7:00 pm, and one drop around 3:00 am. Figure 2 lists the questions that was used to assess the pharmacist's Knowledge of Chronopharmacology of Antihypertensive Medications and the answers by study participants (n=100) 87% of participants agreed that morning dosing of hydrochlorothiazide/captopril is more helpful in reducing the blood pressure as compared to evening medication. In addition 24% of pharmacists in our study did not know whether or not evening dose of nifedipine and GTN was more helpful in decreasing the blood pressure as compared to the early hours in the morning. Concerning patient counseling, majority of pharmacists (72%) agreed that patient counseling should involve verifying patient's knowledge and understanding how to take their medicines. Other aspects also agreed upon by majority of pharmacists including, time of drug administration (73%), providing patient specific printed information (72%), dependence of efficacy and safety of antihypertensive medications on time of administration (72%), and consideration of patient educational and cultural factors (80%). On the other hand, 36% of participants disagreed that some medications can be taken at the patient's preferred time during the day either in the morning or in the evening. Figure 3 displays the patient counseling factors taken into account by pharmacists who participated in our study.

The results of our survey reflected high level of consideration of chronopharmacology by pharmacists when counseling patients about hypertension. When counseling patients about hypertension, 9% of pharmacists mentioned that they show "excellent" consideration of chronopharmacology, while 39% said that they show "very good" consideration of chronopharmacology when counseling their patients. However, answers to knowledge questions revealed lack of adequate knowledge regarding biological rhythms of hypertension and chronopharmacology of antihypertensive Medications, shown in figures 2 and 3 respectively. Interestingly, 13% of our study subjects disagreed that evening doses of ACE inhibitors, enalapril and perindopril as well as ARBs are more effective in lowering blood pressure than morning doses. In addition, nearly half of our sample (46%) did not know that blood pressure has two peaks (around 9 a.m. and 7 p.m.) and one drop around 3 a.m. In addition, nearly one third of our sample disagreed on evening doses for ACEIs, ARBs, and nifedipine GITS. Concerning patient counseling factors taken into account by pharmacists participated in our study, although, the majority (73%) of the pharmacists agreed on description of the best time of drug administration in the morning or evening when counseling the patient, half of them Administration, about (64%) agreed that patients can take their medicines at their preferred time either in the morning or evening. For exploring the chronotherapy of hypertension a number of trials have established the fact that changing the time of treatment rather than the combination of treatment may be a more practical approach to control blood pressure. It is reported that blood pressure be highest at mid-morning and then fall progressively throughout the remainder of the day and rises again during the early hours of the morning before waking. These findings may have important considerations with regard to the therapeutic management of hypertension as well as the scheduling of anti-hypertensive drug administration (Hermida *et al*., 2013 and Minutolo *et al*., 2007). A study in non-dipper patients with chronic kidney disease showed that changing the time of antihypertensive therapy decreased nocturnal blood pressure (Calvo *et al*., 2005).

Conclusion

The study indicated that knowledge and practice of pharmacists regarding the effect of time of drug administration of antihypertensive drugs need further improvement. The improvement can be done by contribution of healthcare professionals and providers to feedback about the appropriate pharmaceutical care provided regarding the importance of patient counseling and chronopharmacology.

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