Global Health
AN ONLINE JOURNAL FOR THE DIGITAL AGE

Syama Priya Thampi, Balakeshwa Ramaiah
Email – drbalakeshawaramaih@gmail.com

Syama Priya Thampi[1], JasonGuy[2], Raju Koneri[1], Dominic Benjamin[3], M. Chandra Sekar[2], Balakeshwa Ramaiah[1]

[1]Department of Pharmacy Practice, Karnataka College of Pharmacy, Bengaluru, [2]College of Pharmacy, University of Findlay, [3]Department of Medicine, Bangalore Baptist Hospital

PHARMACIST MANAGED PROSPECTIVE INTERVENTIONAL STUDY IN THE MANAGEMENT OF HYPERTENSION AT A TERTIARY CARECENTRE IN INDIA

Introduction

Hypertension is one of the most preventable contributors to disease and death. Hypertension is a major risk factor for stroke (ischemic and hemorrhagic), myocardial infarction, heart failure, chronic kidney disease, peripheral vascular disease, cognitive decline and premature death. To help ensure that patients receive quality care, general guidelines have been established to help guide health care professionals to use evidence-based medicine.

These clinical guidelines are an intersection between evidence from data in scientific studies and clinical discussions that when used appropriately can help improve patient outcomes. The Joint National Committee (JNC-8) guidelines are helpful when dealing with patients with hypertension. These guidelines provide evidence-based recommendations for stage 2 hypertension and above, which should meet the clinical needs of many patients. However, the decision regarding the clinical care must be integrated to the clinical needs and circumstances of each individual with the evidence from the guidelines and clinical studies.[1]

By testing and practicing this evidence-based medicine approach using guidelines, healthcare professionals (including pharmacists and pharmacy students) can recommend alternative therapies for patients who are not successful on their current treatment option for approval to the physician. Additionally, in various clinical settings, the compliance of the prescribing pattern in accordance with global recommendations can be analyzed.[2,3] Applying evidence-based guidelines and current primary literature to specific patient situations will help reduce the risk of occurrences of cardiovascular disorders and underlying end organ damage associated with high blood pressure, hence reducing the risk of morbidity and mortality.[3]

A multidisciplinary approach with greater involvement of clinical pharmacists in patient care will improve patient outcome in a cost-effective manner. However, data demonstrating similar effectiveness of pharmacist intervention in improving patient outcome is lacking for the Indian scenario.

This study aimed to measure treatment outcomes by improving medication adherence, analyzing the compliance of prescribing pattern of antihypertensive as per global recommendations, and making patient interventions to improve the quality of life of patients and to help them achieve their health-related goals.[4,5]

Aim

To determine the effect of pharmacist and student pharmacist recommendations on stage 2 hypertension and above at a tertiary care hospital.

Methodology

This prospective study from 2017-2018 was approved by the University of Findlay Institutional Review Board (IRB). The University of Findlay partnered with a tertiary hospital in India to conduct the study. A convenience sampling method utilizing protocols developed at the tertiary hospital were used for this study. All study participants were provided with informed consent before starting the study. The student clinical pharmacist provided medication recommendations to health care professionals and monitored blood pressure changes before and one day after the recommendation to the health care professional. Regular follow-up blood pressure measurements were continued. Patient medical records were reviewed by student clinical pharmacists to identify if a patient was eligible to participate in the study. Recommendations made to health care providers were documented along with the monitoring of blood pressure each day and documented whether recommendations were accepted or not accepted by the physician. Documentation also included the type and nature of recommendation given in terms of drug therapy. A specially designed data collection form was developed to help the student document clinical information. The student clinical pharmacist used JNC 8 guidelines to help provide evidence-based recommendations for patients to help support patientcare.

Study Population Inclusion/Exclusion Criteria

Patients were included in the study if they met the following criteria: >18 years of age requiring inpatient services, hypertensive patients, patients with diastolic blood pressure above159mmHg, and newly presented hypertensive status. Patient's visiting the outpatient department of the tertiary care facility were excluded from the study. Pediatric patients and pregnant women were excluded.

Endpoints

The study evaluated several different endpoints. The first endpoint was change in blood pressure before student recommendation and after student recommendation (Day 1 vs Day 2). A co-primary endpoint was the difference in blood pressure among recommendations that were accepted vs recommendations that were not accepted. In addition, the researchers also evaluated how many recommendations made were accepted by health care professionals and what the major topic areas were for recommendations by student pharmacists.

Statistical Analysis

A sample of 220 patients was followed at the tertiary hospital. A sample size of 126 recommendations was needed to achieve a power of 80% using an alpha of 0.05 assuming a mean blood pressure of 150 mmHg. A t-test was used to compare continuous data for two independent groups. P-values less than 0.05 were considered statistically significant. Descriptive statistics were also used in the analysis. Microsoft Excel v16 and SPSS v25 were used to conduct the analysis of thedata.

Results

Table 1 Patients affected with stage 2 hypertension and above in the sample population		
Stage of hypertension	Number of patients	Percentage (%)
Stage 2	200	90.9
Hypertensive crisis	20	9.1
Total	220	100

Patients affected with stage 2 hypertension are higher compared to that of the patients affected with hypertensive crisis (Table 1). Out of 220 patients enrolled for the study, 200 (90.9%) had stage 2 hypertension with a maximum systolic blood pressure of 190 mmHg and diastolic blood pressure 100 mmHg.

A total of 220 patients were enrolled and monitored for the study by a student clinical pharmacist and supervising pharmacist. 133 recommendations were made, and 120 recommendations were accepted by physicians representing 90% of recommendations (Table 2).

Table 2: Student Clinical Pharmacist's Recommendations & Response	
Total number of recommendations made	133
Number of accepted recommendations	120
Number of rejected recommendations	13

For the group of patients with recommendations made by the student pharmacist and supervising pharmacist, and accepted by the physician, the day 2 average systolic blood pressure was reduced to 150 mmHg and the average diastolic blood pressure to 85 mmHg from an average systolic blood pressure of 173 mmHg and an average diastolic blood pressure of 95 mmHg on day 1. This represents a decrease in systolic blood pressure by 23 mmHg and 10 mmHg for diastolic blood pressure.

For the group of patients with recommendations made but rejected by the physician, the day 2 average systolic blood pressure was 153 mmHg and the average diastolic blood pressure was 86 mmHg, compared to the day 1 average systolic blood pressure of 170 mmHg and the average diastolic blood pressure of 85 mmHg (Table 3). This represented a 17 mmHg decrease in systolic blood pressure and an increase of 1 mmHg of diastolic blood pressure.

Table 3: Changes in blood pressure on day 1 vs. day 2 in the accepted recommendation group vs. rejected group		
	Group 1 mmHg	Group 2 mmHg
Day 1 Average BP	SBP = 173 DBP = 95	SBP = 170 DBP = 85
Day 2 Average BP	SBP = 150 DBP = 85	SBP = 153 DBP = 86

Group – 1 Recommendations Accepted
Group – 2 Recommendations Made, but not accepted

Table 4: Comparison of blood pressure changes between groups				
	Group 1	Group 2	Mean Difference	P-value
Change in SBP [mmHg]	23	17	6	0.02
Change in DBP [mmHg]	10	-1	11	< 0.001

Group – 1 Recommendations Accepted
Group – 2 Recommendations Made, but not accepted

There was a 6 mmHg decrease in average systolic blood pressure and 11 mmHg decrease in average diastolic blood pressure for patients in the group that had their student pharmacist recommendations accepted.

Student recommendations varied by topic, but the most common recommendation made by student pharmacists dealt with drug interactions. Students also made recommendations regarding changes in dosage, substituting or changing a medication, adjusting frequency of a medication, changing the dosage form of a medication, additional drug required, and eliminating a medication not needed. Table 5.

Table 5: Reason for Recommendations

Reason for Student Recommendation	Recommendations Focusing on This Topic
Drug Interactions	39%
Additional Drug Added to Regimen	21%
Dosing Change	19%
Change/Substitution of Medication	12%
Removal of Medication Not Required	4%
Change in Frequency of Medication	3%
Change in Dosage Form	2%
Route Change	0%

Table 6: The drugs that frequently caused ADR in the sample population

Name of the drug	ADR	Number of patients	Percentage
Metoprolol	Hypotension	5	13.15

Clonidine	Hypotension	5	13.15
Metoprolol	Depression	1	2.63
Lasix	Hypokalemia	5	13.15
Metoprolol	Bradycardia	7	18.42
Lasix	Nephrotoxicity	4	10.52
Losartan	Hypokalemia	3	7.89
Piptaz	Urticaria	1	2.63
Piptaz	Hypokalemia	1	2.63
Rifaximin	Anemia	1	2.63
Ceftriaxone	Diarrhoea	1	2.63
Hydrochlorothiazide	Arrhythmia	1	2.63
Aspirin	Bleeding	1	2.63
Tigecycline	Nephrotoxicity	1	2.63
Tramadol	Vomiting	1	2.63

Out of all of the student recommendations, 39% of the recommendations were based on drug interactions (Table 5).

Metoprolol induced bradycardia was reported in 7 patients and clonidine induced hypotension was seen in 5 patients, Metoprolol induced depression was reported in one patient (Rare ADR).[7] Hydrochlorothiazide induced arrhythmia was reported and Lasix induced nephrotoxicity was seen in 4 patients (Table 6).

Discussion

Student pharmacists can be a valuable part of the healthcare team when working with a licensed healthcare professional. The training that students received during their study, as well as during their didactic PharmD curriculum and experiential rotations can create a strong foundation of knowledge, that when supplemented with evidence-based guidelines under supervision of health care

professionals could make recommendations that could improve patient care. This study showcases the ability for student pharmacists to be a valuable member of the healthcare team by producing better blood pressure control.

Student recommendations were able to improve blood pressure outcomes resulting in a significant reduction in both systolic and diastolic blood pressure when compared to patients who had recommendations made but not accepted for their care. The differences in diastolic blood pressure were large at 11 mmHg on average. This enhanced blood pressure control could help improve patient outcomes in the long term.

Physicians in this tertiary care hospital were supportive of this collaboration, and showed greater willingness to work with student pharmacists, as most of the recommendations that were made were accepted that would result in improved patient care.

This study demonstrates the value of students pursuing PharmD [clinical pharmacist] specialization to make medication therapy contributions that results in improved patient outcomes in developing countries, where well-established role for pharmacist is yet to be recognized.

Stephen et al. conducted a prospective observational study on comparisons of various stages of hypertension and it was found that the incidence of stage 2 hypertension (65%) was more than hypertensive crisis (32%).[2] In our study the incidence of stage 2 hypertension was even much greater than hypertensive crisis (9.1%).A prospective observational study by Mohammad et al. reported that a total of 57 ADR'S were detected, documented, assessed and reported during their study period in a sample size of 289 patients. The incidence of ADR was found to be 12%. In the study the 12% of the ADR's were high severity and 49% of ADRS were moderate severity.[6] The authors in this study observed 38 ADR's with a sample size of 220 and an incidence of 17.2%.

A case study conducted by Amir I.A et al. reported episodes of depression and anxiety in an elderly patient treated with low dose metoprolol.[7] In the study by Sharminder et al. reported 138 ADRs in 188 patients subsequent to the use of cardiovascular drugs. In that study the most common ADRs were with beta blockers (metoprolol, 17.8%) and diuretics (11.5%)[8].

In this study 38 out of 220 patients reported to have adverse drug reactions. 13.5% of the study population had metoprolol induced bradycardia and one patient suffered from depression episodes which could be a rare ADR of metoprolol. Lasix induced nephrotoxicity was seen in 10.52% of patients. Mogadro et al. conducted a study looking at hypertension control with a pharmacist intervention program and reported that blood pressure control was higher in the intervention group (P = 0.005) at the end of the study. Significant lower systolic blood pressure (−6.8 mmHg, P = 0.006) and diastolic blood pressure (−2.9 mmHg, P = 0.020) levels were observed in the intervention group. This enhanced blood pressure control can help improve patient outcomes.[9] In this study student clinical pharmacist's recommendations were able to improve blood pressure outcomes resulting in the reduction of both systolic and diastolic blood pressure when compared to patients who had recommendations made but not accepted for their care. There was a 6 mmHg decrease in average systolic blood pressure for patients who were in the group that had their student pharmacist

recommendations accepted (23 vs 17 mmHg, p = 0.02). There were 11 mmHg changes in average diastolic blood pressure for patients who were in the group that had their student pharmacist recommendations accepted. In the present study all recommendations that were made were based on evidence-based guidelines. A prospective observational study conducted by Desais et al. reported that a total of 126 (31%) medicine administration errors (AEs) were observed during the study period. Of these, 72 were incorrect dose administration (either lower or higher than the prescribed), 38 were inaccurate dosing interval (not as per specified time interval), and wrong route of administration (oral instead of another route) was detected in 15 and medicine administration to the wrong patient was observed in one patient.[10]

The authors have reported in the study that 39% of the recommendations made were based on drug interactions, with an additional drug added to regimen representing 21% of recommendations made, and dosing changes representing 19% of recommendations made, and drug substitution 12% of recommendations made.

Limitations

In our study the major limitation was there were barriers to the practice of evidence-based medicine. The gap between the demand for health care and resources available to meet that demand is large, resulting in clinicians having to care of more patients in shorter time. There were shortages of scientific evidence in some cases and even when evidence did exist, there were challenges in applying evidence to the care of specific individual patients.

Additionally, this study was performed in one hospital in India and therefore the external validity of the study is low. This is a pilot study and has laid solid groundwork for additional studies that could be performed in multiple hospitals in India. Since patients could not be randomized in the study there are potential confounding variables that could exist based on patients past medication use.

Conclusion

The overarching finding from this study is that, greater involvement of pharmacists in activities directed towards patients and collaboration with other healthcare professionals within a team environment may improve patient health outcomes and may ultimately affect public health. Pharmacist interventions were effective in reducing systolic and diastolic blood pressure. This report thereby reinforces the pharmacists' role in improving the health care system, leading to superior hypertensive patient outcomes.

Acknowledgment

We would like to express our gratitude to the department of cardiology and medicine, for providing opportunity to execute our research work.

Conflict of interest

The authors declare no conflict of interest.

Abbreviations

ADR: Adverse Drug Reactions**, DI** : Drug Interactions, **QOL:** Quality of life

References

1. PaulA, James, MD, Suzanne Oparil MD,et al.2014 Evidence Based Guidelines For The Management Of High Blood Pressure In Adults Report From The Panel Members Appointed To The Eight Joint

National Committee(JNC8).JAMA.d2013.284427 Published onlineDecember18,2013

2. Stephen M, Hunt J, Siemienczuk J, Pape G, et al. A randomized Controlled Trial of Team-Based Care: Impact of Physician-Pharmacist Collaboration on Uncontrolled Hypertension. J Gen Intern Med.23(12):1966-72.

3. Shogban A, Lundquist L, et al. Student Pharmacists' Clinical Interventions in Advanced Pharmacy Practice Experiences at a Community Nonteaching Hospital. AJPE. 2014; 78(3) Article50.

4. Lancaster J, Grgurich P, et al. Impact of Students Pharmacists on the Medication Reconciliation Process in High-Risk Hospitalized General Medicine Patients. AJPE. 2014; 78(2): Article34.

5. Basak, S. C., & Sathyanarayana, D, et al. Pharmacy Education in India. *American Journal of Pharmaceutical Education*, *74*(4),68.

6. Ali Mohammad, Al-Hajje AH, Atoui F Awada S, et al. Drug-related problems identified by clinical pharmacist's students and pharmacist's interventions. *Ann Pharm Fr*. 2012;70(3):169-172

7. Paul A.K, Michel M, et al. antidepressants, metoprolol and the risk of bradycardia. Ther Adv Psychopharmacol 2012; 2(2):43-49.

8. Amir I.A, Ahmed M, et al .Sleep disorders, nightmares, depressions and anxiety in an elderly patient treated with low dose metoprolol. Elsevier.2010Nov-Dec;(32):646.e5-