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MEDICINE

Prescribing Patterns of Antihypertensive Drugs in Patients Attending Tertiary Care Hospitals in Pakistan

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Abstract

The current study was aimed at examining the prescribing patterns of antihypertensive medications, dispensing time, generic prescribing, drug-drug interactions and to determining whether or not prescriptions are consistent with the recommendations of the Joint National Committee (JNC-8) guidelines. A cross-sectional study was conducted in three tertiary care hospitals among patients of 30 years and more who visited the outpatient departments (OPDs) from January 2018 to September 2018. Prescription patterns were assessed by reviewing the patient's prescriptions, who were attending the OPDs of targeted hospitals during the study duration. Drug interactions in prescriptions were checked by using Micromedex® database to detect incompatible drug combinations. A total of 500 prescriptions were collected that met the criteria for inclusion. The sample data consisted of 57% of males with an average age of 54 years. The average time spent by the patients at the dispensing area was barely 1 min, and no proper counselling had provided them how and when to take medicine. One hundred one drug interactions have been identified in prescriptions. The most frequently first line prescribed drug class was found to be calcium channel blockers 27.8%, followed by 26.1% angiotensin-converting enzyme inhibitor, and 16% vasodilators. The trend observed in double combinations was calcium channel blockers + angiotensin receptor blockers (18.6%) followed by vasodilator + Beta-blockers 14.1%, and Beta-blockers +

Key Points

1. The dispensing time spent in selected hospital pharmacies was approximately 1 min and no appropriate counselling was provided to patients and compliance with the JNC-8 guidelines was average.
2. Drug interactions and pharmacological problems have also been reported. There is a need to train physicians and hire qualified clinical pharmacists to reduce such errors.

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angiotensin-converting enzyme inhibitor 7.1%. The study findings demonstrated average compliance with the JNC-8 guidelines; none of the drug was prescribed by generic name and had very short dispensing time without counselling; approximately 101 minor and major drug-drug interactions were identified. This multi-factorial phenomenon of average compliance with the guidelines must be addressed in order to ensure the rational and quality use of medicines to improve the quality of life of patients.

Keywords Antihypertensive medications · Outpatient · Drug interactions · Noncompliance · The average time

Introduction

Hypertension (HTN) is emerging as one of the most significant public health issues in the world, with currently 1.4 billion adults suffering from it and slightly higher among males [1, 2]. Hypertension prevalence is higher in low middle income countries (LMICs) by 31.5% compared to 28.5% in higher income countries because they share weak and unstable healthcare infrastructure [3]. HTN burden in Pakistan is growing continuously; currently, more than 33% adults above 40 years old are suffering from HTN, and the problem is further plagued by irrational medical practices, patient low knowledge, and adherence issues [4–6].

HTN is defined as the persistent elevation of systolic blood pressure (SBP) of ≥ 140 mmHg and diastolic blood pressure (DBP) of ≥ 90 mmHg in arteries [7]. Throughout the world, HTN poses a significant burden on the health care economics because of its inevitable relationship to several cardiovascular complications [8, 9]. The Joint National Committee (JNC-8) on prevention, detection, evaluation, and treatment of high blood pressure-8 has established goals and standard practicing guidelines for the management of hypertension [9]. The JNC-8 guidance document is the current gold standard evidence-based guideline that may lead to significant improvements in clinical parameters for patients with HTN as recommended worldwide if followed [3]. JNC-8 recommends that the initial choice of treatment for hypertension, i.e., stage I (BP > 20/10 mmHg than the normal pressure) should be ACEIs, ARBs, thiazide diuretic, and CCBs alone or in combination. Start one drug, titrate to the maximum dose, and then add a second drug. Begin two drugs at the same time, as separate pills or combination pill. Initial combination therapy is recommended if BP is greater than 20/10 mmHg above goal. Selection of an antihypertensive drug should be based on the presence or absence of concomitant diseases such as diabetes mellitus, problematic adverse effects of specific drugs, and cost considering overall health benefits to the concerned patient. The overall goal of treating hypertension is to reduce hypertension associated with morbidity and mortality [9].

Prescribing trends define the nature and profile of drug usage, patterns, and compliance with regional, state, or national guidelines, such as uniform prescribing instructions, the use of drugs from the list of essential medicines, and the use of generic drugs [10]. Appropriate prescription has a beneficial effect on adherence and disease prevention. Irrational prescription trend (IPT) happens when an excessive dose, frequency, and duration of an antihypertensive medication is prescribed [11]. Inappropriate delivery of drugs may also result in additional costs incurred by the patient due to inefficient treatment and adverse drug reactions [12]. The lack of progress and the occurrence of adverse drug reactions may contribute to a loss of trust between the patient and the clinician [13]. Elderly people are typically vulnerable to adverse drug reactions due to overdose, as their medication excretion and metabolic organs have been atrophied with aging over time [14]. Prescribing trend surveys provides a clear view of prescribing behavior and helps to classify suboptimal prescribing trends for further review. Prescribing trend assessments of chronic drugs may be believed to be reconciling medications as they can be conducted on a regular basis [15].

To the extent of authors knowledge presently, no study has evaluated the prescribing and dispensing practices in HTN patients of Lahore, Pakistan. Therefore, this study aims to examine the prescribing trends, duration of dispensing time, type of dispensing either generic or brand, and drug-drug interactions in prescriptions of HTN patients attending the outpatient departments (OPDs) of tertiary hospitals in Lahore, Pakistan. We will further analyze whether prescribing practices have been following the JNC-8 guidelines.

Method

The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for cross-sectional studies were used to report this study [16].

Study Design and Study Setting

This cross-sectional study was conducted from January 2018 to September 2018, in three tertiary care public sector hospitals, namely Mayo Hospital, Services Hospital, and Shaikh Zayed Hospital Lahore, Pakistan. The study involved the collection of data from 500 prescriptions of patients in OPDs suffering from HTN.

Ethical Conduct

The required ethical approval was taken from the Ethical Review Boards of the concerned three tertiary care public sector hospitals of Lahore, Pakistan. After providing a written and oral explanation of the study, we took informed consent from the patients. Participants were advised that participation in the study was voluntary and could be canceled at any time.

Inclusion/Exclusion Criteria

Patients were eligible to enroll in the study if they were (1) ≥ 30 years of age; (2) attending regularly OPDs of the hospital; (3) able to understand and converse in Urdu; and (4) taking one or more oral antihypertensive medications daily. Patient diagnosis, laboratory results, and prescribed medications were assessed by reviewing patient medical records. Patients with comorbidities were also included, whereas patients with acute illnesses and cognitive and psychiatric issues were excluded.

Sample Size

The Rao Soft calculator calculated a minimum of 384 mandatory sample size based on 33% prevalence, 5% margin error, and 95% confidence interval [17]. Considering the missed information and errors in data, the sample size was increased by 30% ($n = 116$) and made a final required sample of 500 prescriptions. Based on the universal simple random sampling technique, each HTN patient visiting the hospital was assessed for eligibility to be included in the study.

Data Collection Procedure

Simple random sampling technique was used to collect the data from selected OPDs of hospitals. Authors in the form of groups collected data from all included hospitals. Most of the medicines are provided to patients free of cost from the dispensary of hospitals. Data was collected on predefined questionnaire, including sociodemographic data, prescribed drugs, and duration of total dispensing time and possible drug-related problems were assessed by carefully assessing the patient records and by interviewing the concerned patient. The patients visiting the outpatient departments of the selected hospitals were screened over a duration of 9 months. Drug interactions were assessed by checking the online Micromedex ® database [18]. Micromedex is an evidence-based, multi-database drug search engine that provides summary and in-depth information on drugs (prescription and over-the-counter commercial products), diseases, toxicology, and alternative medicines.

Dispensing time was calculated by directly observing the dispensing process. Each hypertensive medication was categorized into one of the following classes: Angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blocker (ARB), calcium channel blockers (CCB), platelets inhibitors, vasodilators, Beta-blockers, Alpha-blockers, and diuretics.

Statistical Analysis

Statistical analysis was performed using Microsoft Excel 2010 and SPSS version 21. Data were presented as frequencies and percentages.

Results

A total of 500 prescriptions were collected randomly in a duration of 9 months. The demographic and clinical characteristics of patients are given in Tables 1 and 2, respectively.

Majority of the participants were male and had an average age of 51.23 ± 26.12 standard deviation years. Twenty-four cases of prehypertension/pre-HTN, one sixty-one cases of stage 1 hypertension, one twenty-nine cases of stage 2 hypertension, and thirty-six cases of hypertension emergency were reported. The mean systolic blood pressure was 145 mmHg and mean diastolic blood pressure was observed to be 98 mmHg.

The average number of drugs prescribed to each patient was 2.5. Overall, 69% of patients have been prescribed with 1–3 drugs, followed by 28% with 4–6 drugs, and only 2% with 7–8 drugs, respectively. Average dispensing time reported including counselling was 60 s in the range of 40–60 s. Cardiovascular diseases (8.6%) followed by obesity (8%) and diabetes mellitus (4.6%) were the most common comorbid conditions.

Table 3 shows the frequency and relative frequency data for mono and combination therapies against hypertension. As per the present study, most of the physicians prescribed two-drug combination (31.2%) to control blood pressure followed by monotherapy (23.2%), three-drug combination (15.2%),

Table 1 Demographics of patients

	n (%)
Males *n* (%)	286 (57.2)
Females *n* (%)	214 (42.8)
Age groups	
Age group 30–45	137 (27.4)
Age group 46–60	247 (49.4)
Age group > 60	116 (23.2)
No of drugs	
1—3	348 (69.6)
4—6	142 (28.4)
7—8	10 (2.0)
Dispensing time (range in seconds)	40sec–1min 20 sec

Table 2 Clinical parameters of patients

Systolic blood pressure	*n* (%)
Normal (< 120 mmHg)	152 (30.4)
Pre-HTN (120–139 mmHg)	26 (5.2)
Stage 1 HTN (140–159 mmHg)	154 (30.8)
Stage 2 HTN (160–179 mmHg)	132 (26.4)
HTN emergency (≥ 180 mmHg)	36 (7.2)
Diastolic blood pressure	
Normal (< 80 mmHg)	150 (30.0)
Pre-HTN (80–89 mmHg)	24 (4.8)
Stage 1 HTN (90–99 mmHg)	161 (32.2)
Stage 2 HTN (100–119 mmHg)	129 (25.8)
HTN emergency (> 120 mmHg)	36 (7.2)
Comorbidities	
Diabetes mellitus	23 (4.6)
Dyslipidemia	13 (2.5)
Obesity/overweight	40 (8.0)
Renal diseases	21 (4.2)
Cardiovascular diseases	43 (8.6)
Liver diseases	9 (1.8)
Others	13 (2.6)

Table 3 Antihypertensive medication used by hypertensive patients

Treatment	*n* (%)
Monotherapy	116 (23.3)
CCB	32 (27.8)
ACEI	30 (26.1)
Vasodilator	19 (16.5)
Diuretics	17 (14.8)
Double combination	156 (31.2)
CCB + ARB	29 (18.6)
Vasodilator + Beta-blockers	22 (14.1)
Beta-blockers + ACEI	11 (7.1)
Beta-blockers + Alpha-blockers	8 (5.1)
Triple combination	76 (15.2)
Antiplatelet+ antiplatelet + antihyperlipidemics	8 (10.5)
Vasodilator + CCB + diuretics	6 (7.9)
Antiplatelet + antiplatelet + vasodilator	5 (6.6)
Antiplatelet + vasodilator + antihyperlipidemics	5 (6.6)
Four drugs combination	52 (10.4)
Antiplatelet + antiplatelet + vasodilator + antihyperlipidemics	8 (15.4)
Antiplatelet + vasodilator + Beta-blockers + antihyperlipidemics	7 (13.5)
Antiplatelet + antiplatelet + vasodilator + Beta-blockers	6 (11.5)
Antiplatelet + Beta-blockers + antihyperlipidemics + ACEI	5 (9.6)
Combination with other drugs	100 (20.0)

Abbreviations: *ACEI*, angiotensin-converting enzyme inhibitor; *ARB*, angiotensin receptor blockers; *CCB*, calcium channels blocker

and four-drug combination (10.4%), respectively. CCB (27.8%) are the most widely prescribed drugs followed by ACEI (26.1%), vasodilators (16.5%), and diuretics (14.8%) in monotherapy. CCB + ARB (18.6%) were mostly used in two-drug combination therapy followed by vasodilators + Beta-blockers (14.1%) and Beta-blockers + ACEI (7.1%) combination. Antiplatelet + antiplatelet + antihyperlipidemic (10.5%) were mostly used in three-drug combination followed by vasodilator + CCB + diuretics (7.9%).

The average time spent between patient and dispensing area was almost 60 s because there was much load of the patient in dispensing section, so counselling regarding medication was poorly recorded according to this study findings. A total of 101 drug interactions were reported in our study, four of which were of serious nature, while the remaining were minor. The prevalence of major drug interactions was 3.9%, and the prevalence of minor interactions was 96%. Out of a total of 500 prescriptions analyzed, no single generic prescription was observed.

Discussion

The analysis of prescription patterns in LMIC is of paramount importance. The utilization of such surveys not only enables the health care system to perform medical audits but is also responsible for promoting the overall health of the community by initiating a positive transition from traditional regimes to standardized optimized therapeutic plans. The prescription pattern of these antihypertensive drugs was found to be considerately in adherence to the report of Joint National Committee (JNC 8) for the prevention, detection, evaluation, and treatment of hypertension.

Brand prescribing is the preferred practice over the preferable generic prescribing; other studies conducted in Pakistan also reported this finding [19, 20]. Pakistan has an underprivileged society where the majority have limited available financial resources. Physicians need to employ generic prescribing instead of brand prescribing to not only ensure efficient utilization of the already scarce therapeutic resources but also achieve patient cost-effective outcomes. Study results showing that HTN is more prevalent in males than females. This pattern is analogous to the studies conducted in Pakistan [21, 22]. This study also demonstrated that hypertension is more prevalent in elderly patients of age group 46–60, and literature survey also support hypertension is more prevalent in elder patients [23].

Medicine prescribing shows that most frequently prescribed classes of drugs used are (27.8%) calcium channel blockers followed by (26.1%) ACEI, (16%) vasodilators,

and (14.8%) diuretics in monotherapy observed. Our results were different from the American study which reported (29%) ACEI, (24%) diuretics, (22%) ARB, (21%) CCB, and (19%) Beta-blockers [24].

The eighth report of Joint National Committee JNC-8 [9] recommends the use of thiazide diuretic, ACEIs, ARB, and CCBs alone or in combination for the management of early-stage hypertension thus suggesting the trend conforms to the guideline [9]. However, use of vasodilators (16.5%) as first line therapy is not recommended by guideline which our study reported. CCB + ARB (18.6%) were mostly used in two-drug combination therapy followed by vasodilators + Beta-blockers (14.1%) and Beta-blockers + ACEI (7.1%) combination. These two-drug combinations are also suboptimal according to JNC-8 guidelines. Antiplatelet + antiplatelet + antihyperlipidemic (10.5%) were mostly used in three-drug combination followed by vasodilator + CCB + diuretics (7.9%). These two- and three-drug combinations also do not fully follow the JNC-8 guidelines and similarly previous studies conducted in Pakistan also reported this issue [21, 25].

According to our study findings, more than 90% of the patients left the counter without knowing the names of drugs, side effects, and precautions associated with their medications. This may be because most customers do not know about a pharmacist or lack of pharmacist at dispensing area or most of the people belong to rural areas and are illiterate; therefore, they do not know about the drugs they are being treated with.

Drug-drug interactions are one of the most serious problems with drug prescribing as some of the physicians do not have updated knowledge about all significant and clinically meaningful drug interactions moreover they underestimate the risk of co-administration of multiple drugs [26, 27]. Drug interactions are a significant source of patient discomfort and non-adherence to the prescribed therapeutic regimen. Other factors such as patient age, foods, drinks, environmental agents, and genetic factors can also contribute to drug interactions and non-adherence. In addition, the pharmacist rarely intervenes when a potential clinically significant DDI is observed due to their shortage and busy schedule [28]. Research using prescription drugs and checking their interaction from available databases like Micromedex drug can examine and help in drug interaction and their management [29]. The interactions were found to be of significant severity in four cases which were promptly reported to the concerned physicians. The four majorly severe drug interactions which were reported to the concerned physician included, in the first case, an oral anti-diabetic (metformin) that was prescribed to be taken concomitantly with a Beta-blocker. The concomitant administration of a Beta-blocker with an oral hypoglycemic agent has a risk of not only a synergistic hypoglycemic effect but also masking of hypoglycemia symptoms. In the second case, a patient who had been taking digoxin was put on a therapy of thiazide diuretic (chlorothiazide) because the attending physician had failed to notice the patient's medication record. In the third case, it was found that a patient who was prescribed a calcium channel blocker (verapamil) was put on loperamide for diarrhea. The concomitant administration of verapamil and loperamide has the risk of major interaction because verapamil increases the serum levels of loperamide resulting in cardiac arrest. The fourth case also involved the calcium channel blocker (verapamil), and it was prescribed with lovastatin. The simultaneous administration of verapamil with lovastatin has the risk of an elevated serum concentration of lovastatin, resulting in an increased risk of cardiac myopathy development.

Not a single prescription reported generic prescribing which is totally against the guideline. Other studies conducted in Saudi Arabia reported 33% generic prescribing [30] and one possible reason may be the influence of pharmaceutical companies' gifts. Several prescriptions contain more than five drugs, i.e., polypharmacy observed. This is not only the case with prescribing hypertension, but other studies conducted in Pakistan also highlight highly irrational prescribing, such as in angina and asthma [31, 32]. Amer et al. reported that pharmacist education intervention has a positive impact on medication adherence, quality of life, and control of blood pressure in HTN patients [33]. The prospect of continuing medical education should be translated among all hospital departments to maximize awareness about latest therapies launched. In all hospitals, rational prescribing should be prioritized.

Limitations of the Study

The limitations of the study included data containment, i.e., data were collected from only three institutions located in Lahore, Pakistan, and hence, the population is relatively less heterogeneous, not representative of Pakistan as a whole. Therefore, to achieve positive reproducible and credible outcomes, broad studies involving a heterogeneous population from all over Pakistan must be performed. Another limitation of the study was one-point analysis, i.e., no follow-up is conducted. Despite these limitations, the strength of the data collected is such that it revealed several essential aspects of the antihypertensive drug utilization pattern and adherence of these drugs to JNC-VIII guidelines among different comorbid conditions.

Conclusion

The present study concludes that majority of physicians are following JNC-8 guidelines, practicing in the public sector hospitals of Lahore, Pakistan. Thus, most of the patients being treated are receiving the most current evidence-based medicines. Average dispensing time was 1 min that no one in the

hospital pharmacy provided counselling to patients, and this can lead to non-adherence. The findings of this study are very beneficial for Pakistani policymakers in the design of evidence-based approaches, the training of physicians on the JNC guidelines, and the recruitment of pharmacists for therapy and on-prescription rationality tests to enhance patient health outcomes. Rational and scientific efforts to improve drug management systems can only be undertaken in the presence of appropriate and up-to-date information on current practices.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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