

Drug Utilization Of Anti-Diabetic And Anti-Hypertension Drugs At Tertiary Care Teaching Hospital, Bangalore, India

MOHAMMADHADI MOSALLANEZHAD*, SHEKAR H S

Doctor of Pharmacy, Department of Pharmacy Practice, Visveswarapura institute of pharmaceutical sciences, Bangalore, India

*Mail: M.hadimosalla@gmail.com

<https://orcid.org/0000-0002-6738-8084>

<https://orcid.org/0000-0002-8647-9758>

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Abstract

Background: Hypertension is extremely prevalent in patients with diabetes. Limited data exist on utilization patterns of antihypertensive in this population are consistent with evidence-based practice guidelines.

Objective: The present study is aimed to evaluate utilization patterns of antihypertensive agents among hypertensive diabetic patients.

Methodology: The study was conducted in the patient pharmacy department of Bangalore.

A prospective observational study was conducted for a period of 6 months in at Tertiary Care Teaching Hospital, Bangalore, India. We included 150 hypertensive diabetic patients with or without other comorbid conditions and patients aged below 18 years and pregnant women were excluded. All the prescribed medications along with other medications and relevant information will be noted in a customized data collection. The study patients will be followed daily until their discharge. The Micromedex, Medscape, articles and relevant references books will be used as tools to review the collected data. The prescribed medication will be checked for their existence in the hospital and also the reelevant calculation. Check for any error in prescription such as doses, frequency and route of administration and analysis.

Result: Out of 150 patients, 50% were male and 50% were female. Maximum patients belonged to age group of 51-60 years. Chronic Kidney Disease (18%) the was the most common associated disease with hypertension and diabetes mellitus. More than half of the patients had received one antihypertensive drug (60%), followed by two (28%), three (10%) and four (2%) antihypertensive drugs. Amlodipine (CCB) was the most commonly prescribed antihypertensive drug (64%).

Conclusion: Amlodipine and furosemide were the most frequently prescribed antihypertensive drugs. Prescription of antihypertensive drugs for some patients with compelling indications were not in congruent with JNC 8 guidelines. This study highlights some therapeutic rationality in this health center. However, targeted education of the prescription-givers and dissemination of treatment guideline could facilitate rational use of drugs and adherence to treatment guide lines.

Keywords: Hypertension, Diabetes Mellitus, Drug Utilization

INTRODUCTION

According to WHO, Hypertension is defined as a systolic blood pressure (SBP) of 140 mm Hg or more, or a diastolic blood pressure (DBP) of 90 mm Hg or more.[1-4] Drug utilization has been defined as the marketing, distribution, prescription, and use of drugs in society, with emphasis on the resulting medical and social consequences.[5] The principal aim of drug utilization studies (DUS) is to facilitate the rational use of drugs in population. Diabetes

Mellitus (DM) is a most common metabolic disorder characterized by hyperglycemic.[6,7] Diabetes has emerged as a major healthcare problem in India. India has the largest population of diabetes in the world. The international diabetes federation (IDF) estimates the number of people with diabetes in India will reach 80million by the year 2025. A survey depicts that 4% of adults in India suffered from diabetes in the year 2000 and is expected to increase to 6% by the year 2025.[8,9] The world health organization (WHO) has projected that the global prevalence of type-2 diabetes mellitus will more than double from 5 million in 1995 to 300 million by 2025. Between 1995 and 2025, there will be a 35% increase in worldwide prevalence of diabetes mellitus, from 4 to 5.4%. [10-12]

Worldwide prevalence of DM is estimated to rise from 382 million in 2013 to 592 million in 2035.[13,14] The prevalence of type 1 diabetes (T1DM) is about 5% to 10% and type 2 diabetes mellitus (T2DM) is about 90% to 95%. [15,16] There is no specific cause for DM, but both etiologic factors and risk factors are associated with it. The risk factors are heredity, obesity, increasing age, emotional stress, autoimmune β -cell damage, endocrine diseases (e.g. Cushing disease).[17,18] In addition to that the incidence is increasing in rural parts of India due to urbanization, obesity, unsatisfactory diet, sedentary life style, etc.[19,20] Both types of diabetes have microvascular and macrovascular complications.[21-24]

Hypertension is a vital hazard factor for CVD & is a noteworthy worldwide weight on public health. The prevalence of hypertension is high & the prescription containing anti-hypertensive drugs is increasing along with other diseases like diabetes, hyperlipidemia & CVD. The medication usage examines which assess and investigations the medication therapy in HTN & hypertensive diabetic patients is exceptionally basic to observe the prescribing practices of physicians with the point of balanced utilization of medications and to limit the adverse drug reactions (ADRs). Such examinations in this manner help in improving the patient social insurance further. Hence this study is proposed. Hypertension rules from the Eighth Joint National Committee (JNC 8) were published in 2013. In contrast to the JNC7 guideline recommendation, 2014 rule is driven by an efficient review of clinical trial proof and offers a lot of advantages over the previous one. Way of life proposals were likewise distributed in 2013.[25,26] Diabetes and hypertension comprise an especially hazardous combination with regarding cardiovascular grimness and mortality. A significant increment in systolic circulatory strain in any age bunch prompts critical increment in cardiovascular disease. In this manner, it is important to lessen blood pressure.[27,28] Most patients with hypertension and diabetes require more than one authority to accomplish palatable heartbeat control. In the HOT (Hypertension Optimal Treatment) preliminary, 68% of patients were kept up on mix antihypertensive therapy. The mix of ACE inhibitors and CCBs is connected with an abatement in cardiovascular events and protein-urea. [29-32] The combination of a dihydropyridine and a non-dihydropyridine CCB has been appeared to have a synergistic circulatory strain bringing down potential. [33-35] Carefully designed program of physical action can bring down BP. Normal physical activity for at any rate 30 minutes most days of the week is prescribed for all grown-ups. Cigarette smoking, while not thought about an auxiliary reason for basic hypertension, is a major, independent, modifiable hazard factor for CV illness. Patient with hypertension, who smoke ought to be guided in regards to the extra health risks that outcomes from smoking, in addition, the potential advantages that discontinuance can give ought to be disclosed to encourage cessation. fundamental goal of the examination was to assess the pattern of use of anti-hypertensive drugs in patients having diabetes mellitus.

METHODS

It was a prospective, observational study conducted on patients admitted to the Department of Cardiology, Visveswarapura institute of pharmaceutical sciences, who are on antihypertensive and antidiabetic drugs. This was an observational study done using a prospective case notes review methodology. The researcher visited the cardiology department of the hospital daily and reviewed the case records of patients aged 60 years and older who had been admitted on that particular day. Data was collected from the case sheet, medication chart of the patients from the day of admission until the patient was discharged from the hospital. Patient details were entered into a specially designed proforma:

- Patient details like: Name, Age, Sex
- Details of medications currently prescribed - name of the drug (brand and generic), dose, route of administration, duration of therapy

- Any change in the medication therapy during the hospital stay.

ANALYSIS OF THE DOCUMENTED DATA:

- The data collected was analyzed for:
- Number of drugs prescribed to a particular patient during the hospital stay.
- The drugs given was analyzed for prescribing pattern for diagnosis made according to therapeutic classification of the drugs.
- The percentage of drugs prescribed by generic name was calculated.
- The data was evaluated for adverse drug reactions (if any).
- The data was evaluated for any drug-drug interactions (if any).
- The data was analyzed for prescribing pattern of drugs.
- The medication order was assessed for any adverse drug reaction and drug-drug interactions by reference to: Micromedex (drudge), web med and standard text books.

RESULTS AND DISCUSSION

A prospective, observational hospital-based study was carried out in 100 patients who were admitted to the Department of Cardiology at Visveswarapura Institute of Pharmaceutical Sciences, for a period of six months. Among the included patients 39 (39%) were females which were found to be less in number compared to males 61 (61%) patients. TABLE 1

TABLE 1: GENDER WITH CONDITION DISTRIBUTION OF THE STUDY POPULATION				
CONDITION	FEMALE	MALE	TOTAL NUMBER OF PATIENTS(n=100)	PERCENTAGE (%)
TYPE 2 DM	01	04	05	5
HYPERTENSION	14	24	38	38
TYPE 2 DM AND HYPERTENSION	24	33	57	57
TOTAL	39	61	100	100

Considering the gender with condition distribution of the study population .it was found that 5(5%) patients with Type 2 DM, out of which 4 patients were males and 1 patient was female. 38(38%) patients with Hypertension, out of which 24 patients were male and 14 patients were female. 57(57%) patients were found to be both Type 2 DM and hypertensive, out of which 33 were male and 24 were female. TABLE 2

TABLE 2: AGE AND GENDER DISTRIBUTION IN PATIENTS WITH TYPE 2 DM AND HYPERTENSION				
AGE RANGE (IN YEARS)	FEMALE	MALE	TOTAL NUMBER OF	PERCENTAGE (%)

			PATIENTS(n=57)	
60-64	09	12	21	36.84
65-69	11	10	21	36.84
70-74	02	05	07	12.28
75-79	01	04	05	8.77
80 and above	01	02	03	5.26
TOTAL	24	33	57	100

Considering the age with a gender distribution of the study population, it was found that 38 patients were between the age of 60 to 64 years, out of which 25 patients were males and 13 patients were females. 31 patients were found to be between the age of 65 to 69 years, out of which 14 patients were males and 17 patients were females. 16 patients were in the range of 70 to 74 years, out of which 12 patients were males and four patients were females. 10 patients were in the range of 75 to 79 years, out of which seven patients were males and three patients were females. five patients were found to be at the age of 80 years and above, out of which three patients were males and two patients were females.

Considering the age with gender distribution in patients having both type 2 DM and hypertension in the study population. It was found that 21 patients were between the age of 60- 64 years, out of which 12 were males and nine were females. About 21 patients were between the 65-69 years, of which 10 were males and 11 were females. seven patients were between 70-74 years, out of which five were males and two were females. five patients were between 75-79 years, of which four were males and one was female. There were about three patients in the age group of 80 years and above, out of which two were males and one was female.

Considering the age and gender distribution of patients with Hypertension in the study population. It was found that 15 patients were between the age of 60- 64 years, out of which four were females and 11 were males. eight patients were between 65-69 years, of which five were females and three were males. nine patients were found between 70-74 years, out of which two were females and seven were males. four patients were between 75-79 years, of which two were females and two were males. There were about two patients at the age group of 80 years and above, out of which one was female and one was male.

Considering the age with gender distribution of patients with Type 2 DM in the study population. It was found that two patients were between the age of 60- 64 years who were males. two patients were between 65-69 years, of which one was female and one was male and there was only one male patient between 75-79 years.

We found the utilization pattern of antidiabetic drugs in 62 patients with Type 2 DM. about 110 prescriptions were prescribed for antidiabetic drugs. Out of which 29 prescriptions were for sulfonyl urea of which 28(25.45%) prescriptions were for glimepiride and one (0.90%) prescription for gliclazide, biguanide 40(36.36%) prescriptions were for metformin. Frequency of Alpha glucosidase inhibitors prescribed was two (1.81%) voglibose, six prescriptions were for dipeptidyl peptidase -4 of which five (4.54%) prescriptions were for teneligliptin and one (0.90%) prescription for sitagliptin. In this study population frequency of human regular insulin was 33 (30.00%). Considering the distribution of the antidiabetic drugs prescribed in 62 patients. Out of 62 patients, 34 patients received monotherapy and 28 patients received combination therapy. According to prescribing pattern, 43.54% of patients were prescribed with monotherapy. 35.48% patients were prescribed with two drug combination, 14.51% patients were prescribed with three drug combination and 4.83% patients were prescribed with four drug combination. We identified Metformin and Insulin were the anti-diabetic drugs that were most commonly prescribed in monotherapy. This study reported that frequency of prescription for Metformin was 7 and Insulin was 21 as monotherapy treatment for patients with diabetes. The table shows two drug combination therapy included [Gliclazide + Insulin] (1), [Glimipride+ Metformin] (16), [Insulin+ Metformin] (3), [Teneligliptine+ Metformin] (2). Three drug combination therapy included [Glimepiride+ Insulin+ Metformin] (7), [Glimipride+Teneligliptine+ Metformin] (1), [Glimipride+ Voglibose+ Metformin] (1). Four drug combination included [Glimepiride+ Insulin+ Metformin+ Teneligliptine] (2), [Glimepiride+ Voglibose+ Metformin+ Sitagliptin] (1). [Glimepiride+ Metformin] combination was commonly used as two drug combination in 16

prescriptions. [Glimepiride+ Insulin+ Metformin] combination was commonly used as three combination therapy in 7 prescriptions. Monotherapy (28) and two drug combination (22) were used more frequently than three (9) and four (3) combination drug therapy in this study population. We found the frequency of insulin in combination with oral antidiabetic drugs prescribed in the study population. Here the table shows two drug therapy involved [insulin + metformin] (3) and [insulin+ gliclazide] (1), three drug combination [insulin+ glimepiride+ metformin] (7) and four drug combination included [insulin+ glimepiride+ metformin+ teneligliptin] (2). The use of insulin in three drug combination therapy (7) was more when compared to other combination therapies. This shows that insulin was commonly prescribed along with metformin and glimepiride. TABLE 3,4 and 5

TABLE 3: UTILIZATION PATTERN OF ANTIDIABETIC DRUGS IN THE STUDY POPULATION WITH TYPE 2 DM				
CLASS OF ANT DIABETIC DRUGS	TOTAL NUMBER OF DRUGS IN EACH CLASS	ANTI DIABETIC DRUGS	FREQUENCY OF PRESCRIPTION (N=110)	PRESCRIBING PERCENTAGE (%)
BIGUANIDE	40	Metformin	40	36.36
INSULIN	33	Human Regular Insulin	33	30.00
SULFONYL UREAS	29	Glimepiride	28	25.45
		Gliclazide	01	0.90
DIPEPTIDYL PEPTIDASE-4 INHIBITORS	06	Teneligliptin	05	4.54
		Sitagliptin	01	0.90
ALPHA-GLUCOSIDASE INHIBITORS	02	Voglibose	02	1.81
TOTAL	110		110	99.96

TABLE 4: UTILIZATION PATTERN OF COMBINATION OF ANTIDIABETIC DRUGS PRESCRIBED FOR PATIENTS WITH TYPE 2 DM		
DRUG THERAPY	NUMBER OF PATIENTS (n=62)	PERCENTAGE (%)
MONOTHERAPY	28	45.16
TWO DRUG COMBINATION	22	35.48
THREE DRUG COMBINATION	09	14.51
FOUR DRUG COMBINATION	03	4.83
TOTAL	62	99.98

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TABLE5: UTILIZATION PATTERN OF DIFFERENT ANTIDIABETIC DRUGS PRESCRIBED IN COMBINATION FOR PATIENTS WITH TYPE 2 DM

DRUG THERAPY	ANTIDIABETIC DRUGS	FREQUENCY OF PRESCRIPTION (n=62)	PERCENTAGE (%)
MONO THERAPY	Insulin	21	33.87
	Metformin	07	11.29
TWO DRUG COMBINATION	Gliclazide+Insulin	01	1.62
	Glimepiride+Metformin	16	25.80
	Insulin+Metformin	03	4.83

	Teneligliptine + Metformin	02	3.22
THREE DRUG COMBINATION	Glimepiride+Insulin +Metformin	07	11.29
	Glimepiride+ Teneligliptine+ Metformin	01	1.62
	Glimepiride+Voglibose +Metformin	01	1.62
FOUR DRUG COMBINATION	Glimepiride+Insulin +Metformin +Teneligliptine	02	3.22
	Glimepiride+Voglibose+ Metformin+Sitagliptin	01	1.62
TOTAL		62	99.99

We identified the ten different class of anti-hypertensive drugs prescribed. Diuretics was the most frequently prescribed class of drugs of which, spironolactone (13.58%) was the most prescribed diuretic followed by furosemide (13.24%) and torsemide (8.68%), chlorthalidone (1.39%), hydrochlorothiazide (1.04%), metolazone (0.34%) and eplerenone (0.34%). Beta adrenergic blocker were the next most prescribed class where metoprolol (21.25%) was the most frequently prescribed followed by atenolol and timolol maleate (0.34%). Angiotensin receptor blocker was the next most prescribed class where telmisartan (14.98%) was the most prescribed drug of this class. Also, in the vasodilator class, nitroglycerin (8.71%) was prescribed more in this study population continued by isosorbide dinitrate (4.52%), glyceryl trinitrate (2.09%). Calcium channel blocker was next most prescribed class of drug which amlodipine

(3.48%). Alpha –beta adrenergic blocker was next which labetalol (1.39%) was a drug prescribed in this class. Alpha adrenergic blocker was next which silodosin and tamsulosin (1.04%), prazosin (0.34%) were prescribed in this class. Drug prescribed from centrally acting sympatholytic agent was cilnidipine (1.04%). last class of antihypertensive drug was ACE-inhibitor which Ramipril (0.69%) was the drug prescribed in the study population.

We identified the utilization pattern of antihypertensive drugs prescribed. Out of 95 patients with hypertension, 24 patients received monotherapy and 71 received combination therapy. In this study, antihypertensive drugs were also prescribed as combination therapy which includes two drug combination 30(31.57%), three drug combination 22(23.15%), four drug combination 12(12.63%), five drug combination 4(4.21%) and six drug combination 3(3.15%). The study showed that two drug therapy (31.57%) was the most frequently prescribed. The next most prescribed was monotherapy (25.26%) followed by three drug combination therapy (23.15%).

Considering the utilization pattern of different antihypertensive drugs prescribed as monotherapy for 24 patients with hypertension. Diuretic (16) was the most frequently prescribed followed by beta adrenergic blocker (7) and angiotensin receptor blocker (1).

We identified the two-drug combination therapy in the descending order of their prescription pattern:

[beta adrenergic blocker+ vasodilator] (9), [diuretic+ vasodilator] (4), [angiotensin receptor blocker+ diuretic] (4), [angiotensin receptor blocker+ beta adrenergic blocker] (4), [diuretic+ centrally acting sympatholytic agent] (4), [alpha adrenergic blocker+ vasodilator] (1), [diuretic+ beta adrenergic blocker] (1), [beta adrenergic blocker+ vasodilator] (1), [ACE inhibitor+ diuretic] (1), [diuretic+ alpha adrenergic blocker] (1), [angiotensin receptor blocker+ vasodilator] (1).table6

TABLE 6: UTILIZATION PATTERN OF DIFFERENT ANTIHYPERTENSIVE DRUGS PRESCRIBED IN TWO DRUGS COMBINATION FOR PATIENTS WITH HYPERTENSION			
DRUG THERAPY	ANTIHYPERTENSIVE DRUGS (BY CLASS)	FREQUENCY OF PRESCRIPTION (n=31)	PERCENTAGE (%)
TWO DRUG COMBINATION	Beta Adrenergic Blocker + Vasodilators	09	29.03
	Angiotensin Receptor Blocker+ Beta Adrenergic Blocker	04	12.90
	Angiotensin Receptor Blocker + Diuretic	04	12.90
	Diuretic+ Centrally Acting Sympatholytic Agent	04	12.90
	Diuretic + Vasodilators	04	12.90
	Alpha Adrenergic Blocker+ Vasodilators	01	3.22
	Diuretic+ Beta Adrenergic Blocker	01	3.22
	Beta Adrenergic Blocker + Vasodilators	01	3.22
	Ace Inhibitors+ Diuretic	01	3.22
	Diuretic+ Alpha Adrenergic Blocker	01	3.22
	Angiotensin Receptor Blocker+ Vasodilator	01	3.22
TOTAL		31	99.95

Considering the three drug combination therapy follows [angiotensin receptor blocker+ diuretic+ beta adrenergic blocker] (7),[angiotensin receptor blocker+ beta adrenergic blocker+ vasodilator] (6), [angiotensin receptor blocker+ Ca channel blocker+ beta adrenergic blocker] (1), [angiotensin receptor blocker+ diuretic+ vasodilator] (1),[angiotensin receptor blocker+ Ca channel blocker+ diuretic] (1), [Ca channel blocker+ diuretic+ beta adrenergic blocker](1), [diuretic+ beta adrenergic blocker+ vasodilator] (4),[ACE inhibitor+ diuretic+ beta adrenergic blocker] (1). This study reported that the combination of [angiotensin receptor blocker+ diuretic+ beta adrenergic blocker] (7) was higher and the next most prescribed combination was that of [angiotensin receptor blocker+ beta adrenergic blocker+ vasodilator] (6).

Considering the five-drug combination therapy follows [angiotensin receptor blocker+ diuretic+ beta adrenergic blocker+ alpha adrenergic blocker+ vasodilator] (2). [angiotensin receptor blocker+ Ca channel blocker+ beta adrenergic blocker+ centrally acting sympatholytic agent+ vasodilator] (1), [angiotensin receptor blocker+ Ca channel blocker+ diuretic+ beta adrenergic blocker+ vasodilator] (1).

This study reported the five-drug combination therapy of [angiotensin receptor blocker+ diuretic + beta-adrenergic

blocker+ alpha-adrenergic blocker + vasodilator] (2) was mostly prescribed.

Considering the six-drug combination therapy follows [angiotensin receptor blocker+ Ca channel blocker+ diuretic+ beta-adrenergic blocker+ alpha-adrenergic blocker+ alpha-beta adrenergic blocker] (1), [angiotensin receptor blocker+ Ca channel blocker+ diuretic+ beta-adrenergic blocker+ alpha-beta adrenergic blocker+ vasodilator] (2). The combination of [angiotensin receptor blocker+ Ca channel blocker+ diuretic+ beta-adrenergic blocker+ alpha-beta adrenergic blocker+ vasodilator] (2) was the most commonly prescribed of six combination therapy in this study population. TABLE 7

TABLE 7: UTILIZATION PATTERN OF DIFFERENT ANTIHYPERTENSIVE DRUGS PRESCRIBED IN FIVE DRUGS COMBINATION FOR PATIENTS WITH HYPERTENSION			
DRUG THERAPY	ANTIHYPERTENSIVE DRUGS (BY CLASS)	FREQUENCY OF PRESCRIPTION (N=4)	PERCENTAGE (%)
FIVE DRUG COMBINATION	Angiotensin Receptor Blocker+ Diuretic+ Beta Adrenergic Blocker+ Alpha Adrenergic Blocker + Vasodilator	02	50
	Angiotensin Receptor Blocker+ Calcium Channel Blocker+ Beta Adrenergic Blocker+ Centrally Acting Sympatholytic Agent+ Vasodilator	01	25
	Angiotensin Receptor Blocker +Calcium Channel Blocker + Diuretic+ Beta Adrenergic Blocker+ Vasodilator	01	25
TOTAL		04	100

Considering drug-drug interactions between the drugs prescribed to the patients under study (n=100), (6.73%) of which are serious drug-drug interactions, the detail of this category along with their clinical effects have mentioned in Table 15. (75.96%) of drug-drug interactions were found to be monitor closely interactions and minor drug-drug interactions were found to be (17.03%) in our study.

CONCLUSION

DUE studies, patients will receive medicine appropriate to their clinical needs, in doses to meet their own requirements for an adequate period of time, by this, we can avoid the irrational use of drugs in elderly patients.

The elderly population consumes a disproportionate share of prescriptions and drugs as compared to younger persons. These factors combined with age-related changes in pharmacokinetic and pharmacodynamics parameters make the elderly population more susceptible to drug interaction. Therefore, when the elderly receives drug therapy, it must be necessary for well-defined goals and given at the lowest effective dose to achieve. Drug-drug interactions may be avoided with the discontinuation of drugs that do not achieve the desired endpoints or that are no longer needed.

According to the study, more males were admitted than females. Hence the majority of drug utilization was by males. Hypertension was more prominent in patients than diabetes. ACE inhibitors, Angiotensin receptor blockers, Calcium channel blockers, Diuretics, Beta-adrenergic blockers, Alpha-adrenergic blockers, Alpha-Beta adrenergic blockers, centrally acting sympatholytic agents, and Vasodilators are the most commonly prescribed antihypertensive class of drugs. Sulfonylureas, Biguanide, Alpha-glucosidase inhibitors, Dipeptidyl peptidase-4 inhibitors, and Insulin are most commonly prescribed antidiabetic class of drugs. Polypharmacy has a very high prevalence among hospitalized patients and represents an urgent public health issue that should be addressed. In 28 antidiabetics and antihypertensive drugs for our study population, 104 drug-drug interaction was found in which monitor closely was the most DDI. Considering the adverse outcomes associated with polypharmacy, including adverse drug events, drug-drug interactions, increased cost of medications, increased risk of hospitalization, non-compliance, and various medication errors, polypharmacy must be viewed seriously and steps must be taken to reduce it. Health care professionals should be aware of the risks and should cut down unnecessary medications to prevent polypharmacy from occurring.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available within the article.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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