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Araştırma Makalesi / Research Article

Prescription Pattern and Potential Drug-Drug Interactions of Antihypertensive Drugs in a General Hospital, South Ethiopia

Bir Güney Etiyopya Devlet Hastanesinde Antihipertansif İlaçların Potansiyel İlaç-İlaç Etkileşimi ve Reçete Yazma Modelleri

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ABSTRACT

Purpose: Selection and use of anti-hypertensive agents are not usually compliant with international guidelines. A prescription based survey is the most effective method to assess and evaluate the prescribing pattern of physicians and dispensing practice of pharmacists; hence, the aim of this study was to assess the prescription pattern of anti-hypertensive drugs in Durame General Hospital.

Material and Methods: A retrospective study was carried out from January to February, 2013 on one year patient cards. Records of 250 patients were selected by simple random sampling technique. However, since some of prescriptions are illegible and incomplete, 205 patient records were included in the study.

Results: Out of 205 patients, 46 (22.44%) of them were on mono-therapy and 159 (77.56%) on combination therapy. Among patients on combination therapy, 120 (75.5%) and 39(24.5%) were on two and three drugs combination, respectively. Diuretic was the most frequently prescribed drug both as a single agent (65.22%) and as combination therapy (86.8%). Combination therapy significantly reduced blood pressure as compared to mono-therapy. The majority of co-prescribed drugs which have a potential drug interaction with anti-hypertensive agents were NSAIDs (98.21%).

Conclusion: Combination therapy was the most prescribed pattern to treat hypertensive patients which is in line with international guidelines. However, majority of patients in pre-hypertensive stage were treated by combination therapy which is not recommended. Hence, physicians should consider when the combination drugs are to be prescribed for hypertensive patients.

Key words: Antihypertensive drugs, mono therapy, combination therapy, prescription pattern.

ÖZET

Amaç: Antihipertensif ajanların seçimi ve kullanımı genellikle uluslararası yönergeler ile uyumludur. araştırmaya dayalı ilaç yazma, hekimlerin ilaç yazma şeklini ve eczacıların ilaç hazırlama çalışmasını değerlendirme ve belirlemek için en etkili metoddur, böylece bu çalışmanın amacı, Durame Devlet hastanesinde anti-hipertensif ilaçların ilaç yazma şeklini belirlemekti.

Materyal ve Metod: Geriye yönelik bir çalışma yıllık hasta dosyaları üzerinde 2013 ocak ayından şubat ayına kadar yapıldı. 250 hastanın kaydı basit rastgele örneklem tekniği ile seçildi. ancak bazı reçeteler okunaksız ve eksik olduğu için, 205 hasta kaydı çalışmaya dahil edildi.

Bulgular: 205 hastanın 46'sı (%22.44) mono terapi altındayken, 159'u (%77.56) birleşik tedavi altındaydı. birleşik tedavi altında olanlar arasında 120'si (%75.5) ve 39'u (%24.5) sırasıyla 2 ve 3 ilacı birlikte almaktaydı. diüretik hem tekli ajan tedavisinde (%65.22) hem de birleşik tedavide (%86.8) en sık reçetelenen ilaçtı. birleşik terapi, tekli terapi ile

karşılaştırıldığında kan basıncını önemli derecede azalttı. antihipersensitif ajanlar ile ilaç etkileşiminde olan birlikte yazılan ilaçların büyük çoğunluğu NSAID'lardı.(%98.21).

Sonuç: Yüksek tansiyonlu hastaları tedavi etmek için, birleşik tedavi uluslararası yönerge ile uyumlu olan en çok yazılan reçete şeklidir. ancak, ön hipertensif aşamadaki hastaların çoğu, tavsiye edilmeyen birleşik terapi ile tedavi edildi. böylece doktorlar birleşik ilaçların yüksek tansiyonlu hastalar için yazmak üzerinde olduklarında göz önünde bulundurmalılar.

Anahtar kelimeler: Antihipertensif ilaçlar, mono terapi, combination terapi, reçete yazma şekli

INTRODUCTION

Hypertension is one of the most common worldwide chronic diseases affecting humans. It is a disease of complex etiology, affecting about one billion people worldwide in 2000 and this will be projected to 29.2% (1.5 billion) by 2025[1]. Hypertension was thought to be rare in Africa, but it is now recognized as one of the most important cardiovascular diseases[2-5]. Recent studies from rural areas in sub-Sahara Africa suggest that the prevalence of hypertension is increasing in rural populations[6-9]. Its prevalence in urban areas is practically as high as that in the developed world, ranging from 5% to 20% overall[10]. According to the health and health-related indicators of Ministry of Health, hypertension accounted for 1.4 percent of all deaths reported in Ethiopia in 2008[11].

There are problems for the selection of antihypertensive agents by considering compelling induction and special consideration while the main goal of antihypertensive therapy is to achieve target blood pressure; this selection of agents for an individual should also accounts complicity[12]. The seventh report of the joint national committee on prevention, detection, evaluation, treatment of high blood pressure (JNC 7) and 2007 European society of hypertension-European society of cardiology (ESH-ESC) guidelines recommend the use of combination therapy, which should usually include thiazide diuretics as first line therapy for stage two hypertension and for patient with compelling indication[13,14]. The European guideline, on the other hand, suggests that unless a special indication exists, any of the five antihypertensive classes can be used as first-line treatment[14].

A prescription based survey is considered to be one of the most effective methods to assess and evaluate the prescribing attitude of physicians and dispensing practice of pharmacists[15]. Hence, this study was designed to evaluate prescribing pattern of antihypertensive drugs by physicians, identify co-morbid conditions and other patient parameters related to hypertension at Durame Hospital, South Ethiopia.

METHODS and MATERIAL

Study setting and Design

A retrospective cross-sectional study was conducted on one year patient record data between January, 2012 and February, 2013 in Durame Hospital, South Ethiopia which is 360 km away from Addis Ababa, the capital city of the country. The hospital has different services such as inpatient service, outpatient service, surgical service, gynecology and obstetrics, radiology, pharmacy and laboratory services. For the present study records of 250 patients were selected by simple random sampling technique using table of random numbers. But, forty five patient records were excluded from the study because of illegible and incomplete prescriptions. Hence, 205 patient records were involved in the study.

Data collection

Data collection format/ tool was designed and used by the investigators to collect data and information. To assure the quality of data the checklist or format was pretested and clarity of language of check lists was checked; every day the collected data was reviewed and checked for completeness. Demographic and clinical information including age, gender, documented blood pressure, the anti-

hypertensive medications and other information were recorded.

Data analysis

All the data were analyzed in order to assess the drug utilization in hypertensive patients, to evaluate the prescription pattern, and other illness associated with hypertension. For the purpose of analyzing the prescribing patterns of antihypertensive drugs in the treatment of hypertension the pharmacotherapy was classified as mono-therapy, dual therapy, and triple therapy where one antihypertensive, two antihypertensive and three antihypertensive drugs were respectively used for the treatment. Data was analyzed using Statistical Package for Social Sciences (SPSS) 16.0. Differences between means of two groups were compared using student's *t* test, while that between proportions were compared using chie square test. A p-value less than 0.05 was considered as significant. The results were presented using tables and figures.

RESULTS

The results revealed that out of 205 patient cards selected for the study, more than half of hypertensive patients were females (57%) and the majority of them (63%) were in the age group of 35-54 years. The prevalence of hypertension was more in male patients in age group of 45-64 than other age groups (Table 1).

Table 1. Sex and age distribution of hypertensive patients

		Age						
		<25	25-34	35-44	45-54	55-64	>65	Total
Sex	Male	2 (2%)	10 (11%)	16 (18%)	24 (26%)	23(25%)	16(18%)	91 (44%)
	Female	3 (3%)	12 (11%)	40 (35%)	32 (28%)	19(17%)	8 (7%)	114 (57%)
	Total	5 (2%)	22 (11%)	56 (27%)	55 (27%)	43(21%)	24(12%)	205(100%)

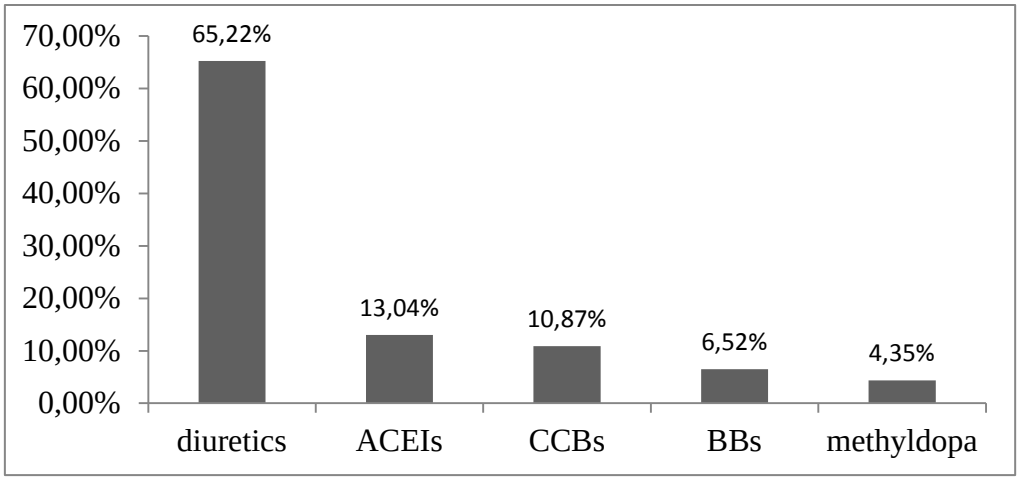

Figure 1. Distribution of antihypertensive drugs prescribed as mono therapy

A total of 46 ant-hypertensive drugs were prescribed as mono therapy during the study period. Out of which diuretics were the most prescribed drugs (65.22%), followed by ACEIs (13.04%) and CCBs (10.87%) (Figure No1).There was no significant difference in baseline blood

pressures of patients on ACEs and those on diuretic mono therapy (P>0.05). However, ACEIs mono therapy significantly lowers blood pressures than diuretic mono therapy (p<0.01)(Table2).

Table 2. Comparison of patients on angiotensin converting enzyme inhibitors mono therapy and diuretic mono therapy

Blood pressure (mmHg)	ACEIs mono therapy	Diuretic mono therapy	t- value	p-value
Baseline mean SBP	156.67±13.91	150±12.64	1.839	>0.05
Baseline mean DBP	97.13±7.15	93.92±5.79	1.949	>0.05
Mean reduction in SBP	20.33±7.76	14.20±6.02	3.247	<0.01
Mean reduction in DBP	11.50±8.15	5.71±4.52	3.447	<0.01

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BP: blood pressure

Patients who were on combination therapy were 159(77.57%). From these, 120 and 39 patients were on dual and triple therapy, respectively. Out of 120 patients to whom two antihypertensive drugs were prescribed, the most frequently used drug combinations were diuretics with ACEIs (32.07%) followed by Diuretics with BBS (17.61%). Among the total patients who were on three antihypertensive therapy (24.5%), about 18 (11.32%) of them were on diuretics with calcium channel blockers and ACEIs while 13 (8.18%) of patients were on combination of ACEIs, Beta blockers and Diuretics. The percentage of diuretics prescribed as a combination was 86.8% (Table 3).

Out of 120 patients on dual therapy, most of them belonged to pre-hypertensive stage (30.73%) followed by stage I(23.41.36%) and stage II(4.39%) hypertension. The majority of stage I hypertensive patients (23.41%) were on dual therapy followed by triple therapy (8.78%) and mono therapy (7.31%). Most of stage II hypertensive patients were on mono therapy (8.78%) (Table 4).

Table 3. Pattern of prescribed antihypertensive drug as combination therapy

Drug regimen	**Frequency**	**Percent (%)**
Two drugs	120	75.5
ACEISs +Diuretics	51	32.07
Diuretics +BBs	28	17.61
Diuretics +CCBs	14	8.80
ACEIs +BBs	12	7.55
BBs +CCBs	9	5.66
Diuretics + α methyldopa	6	3.77
Three drugs	39	24.5
ACEIs +CCBs+ Diuretics	18	11.32
ACEIS +BBs + Diuretics	13	8.18
BBs +CCBs + Diuretics	8	5.03
Total	159	100

ACEIs: angiotensin converting enzyme inhibitors, BBS: beta blockers, CCBs: calcium channel blockers

Table 4. Distribution of patient on mono therapy and different regime of combination therapy

Blood pressure (mmHg)	Therapy			
	Mono therapy	**Two drug combination**	**Three-drug combination**	**Total**
Pre- hypertension (120-139)	13 (6.34%)	63 (30.73%)	13 (6.34%)	89 (43.41%)
Stage I (140-159)	15 (7.31%)	48 (23.41%)	18 (8.78%)	81 (39.51%)
Stage II (>160)	18 (8.78%)	9 (4.39%)	8 (3.9%)	35 (17.07%)

There was no significant baseline blood pressures difference in pre-hypertensive stage patients who were on mono therapy and combination therapy (P>0.05). However, there were significant baseline blood pressures differences in stage one and two hypertensive patients who were on mono therapy and combination therapy (P<0.05). In both stages I and II hypertension as the blood pressure increased, the number of the drugs prescribed also increase. Combination therapy achieved significantly more reduction in systolic and diastolic blood pressures in all hypertension stages than mono therapy (P<0.001) (Table 5).

Table 5. Comparison of patients on mono therapy and combination therapy based on classification of Jnc-7 hypertension guidelines.

Blood pressure (mmHg)	Mono therapy	Combination therapy	t-value	p-value
Pre- hypertension (SBP= 120-139)				
Baseline mean SBP	139.39±4.70	132.57±12.09	0.821	>0.05
Baseline mean DBP	85.23±2.18	85.95±2.18	1.822	>0.05
Mean reduction in SBP	9.52±8.35	18.34±11.93	4.899	<0.001
Mean reduction in DBP	5.29±5.54	9.60±7.15	3.969	<0.001
Stage I (SBP= 140-159)				
Baseline mean SBP	150.21±6.24	152.11±4.10	2.166	<0.05
Baseline mean DBP	93.00±2.48	95.19±1.86	6.072	<0.001
Mean reduction in SBP	16.29±10.63	24.71±11.40	5.151	<0.001
Mean reduction in DBP	6.65±5.62	11.43±7.06	5.231	<0.001
Stage II (SPB ≥ 160)				
Baseline mean SBP	163.68±4.36	173.76±5.92	4.842	<0.001
Baseline mean DBP	104.15±3.67	110.79±4.68	4..705	<0.001
Mean reduction in SBP	20.32±12.27	32.91±10.07	5.575	<0.001
Mean reduction in DBP	12.71±3.12	19.53±4.17	4.348	<0.001

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BP: blood pressure

A total of 164 patients were taking other drugs concomitantly with anti-hypertensive drugs. The most frequently used concomitant drugs were NSAIDs 70(42.68%), antibiotics 38(23.17%), gastro intestinal drugs 30(21.28%), anti-diabetics 8(4.44%) and anti-asthmatic drugs 8(4.44%)(Figure 2).Parts of these drugs have a potential to interact with antihypertensive agents. The majority of co-prescribed drugs that have a potential drug-drug interaction with anti-hypertensive agents were NSAIDs 76(98.70%). Insulin was also prescribed for one patient along with HCT (Table 6).

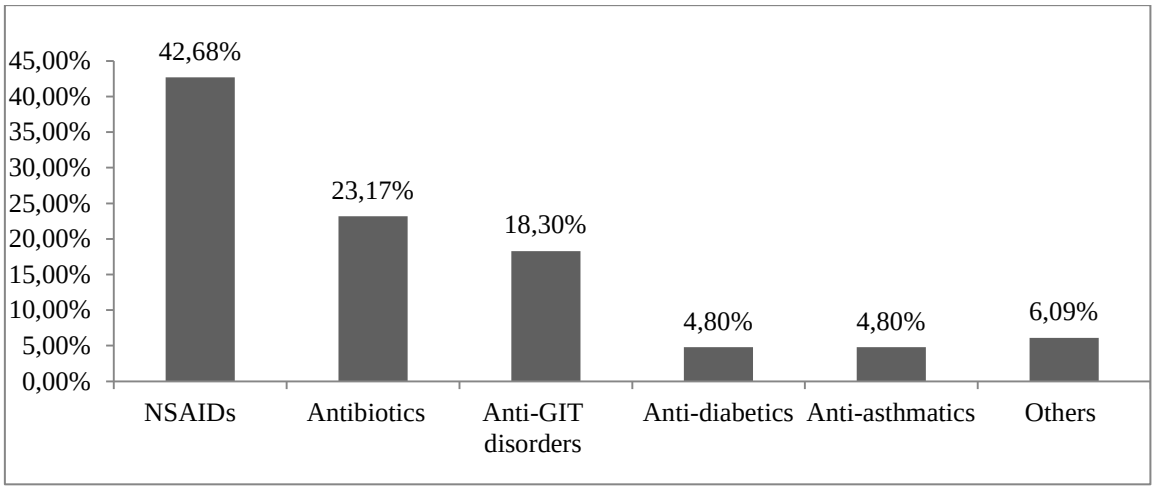

Figure 2. Other drugs concomitantly taken with antihypertensive agents

Table 6. Co-prescribed drugs with antihypertensive agents having a potential drug interaction

Antihypertensive agents	Co-prescribed drugs	No (%)	Antihypertensive agents	Co-prescribed drugs	No (%)
HCT	Aspirin	10(17.86)	Atenolol	Aspirin	4 (7.14)
Enalapril	Aspirin	9 (16.07)	Atenolol	Diclofenac	3 (5.36)
HCT	Diclofenac	9 (16.07)	HCT	Insulin	1 (1.78)
Enalapril	Diclofenac	6 (10.71)	Enalapril	Indomethacin	1 (1.78)
Captopril	Diclofenac	6 (10.71)	HCT	Ibuprofen	1 (1.78)
Captopril	Aspirin	5 (8.93)	Captopril	Indomethacin	1 (1.78)
Total					**56 (100)**

HCT: hydrocortisone thiazide

DISCUSSION

In the present study there were relatively a high number of female patients (55.6%) which is in line with the previous studies wherein more than half of patients were females[16- 18]. This could be associated with pregnancy induced hypertension, high fat accumulation and estrogen level, and less physical exercise practiced by women[19].

The proportion of patients on combination therapy was 77.56% in this study. This observation is similar with the values of Ibadan, Nigeria (73%) [20], but higher than the finding (56%) reported by

Ezuo and Njoku[21]. Moreover, these finding is consistent with the current trends advocating the use of combination therapy as first line treatment[13,14,22]. The high prescription rate of combination therapy might indicate the high prevalence of patients with severe and moderate hypertension, and the presence of co-morbid diseases.

However, there were more patients on combination therapy (37.1%) among pre-hypertensive stage patients. Prescribers might not recognize the negative impact of the practice of poly pharmacy or use of combination of two or more drugs even though the diseases can be managed by single drug and /or life style modifications. This may increase the possible occurrence of the side effects and reduce patient adherence to anti-hypertensive therapy[23].

Moreover, it was observed that combination therapy were more effective than mono therapy in all stages of hypertensive patients. This is in line with the finding reported by Etuk and coworkers[24]. It was also found that ACEIs significantly reduced both systolic and diastolic blood pressure compared to diuretics in patients who received single drug. The advantage of use of ACEIs is in preventing cardiovascular events and target organs disease in patients with diabetes mellitus, heart failure, hypertensive renal insufficiency and diabetic nephropathy[25].

Among patients who were on mono therapy, the majority of them (65.22%) were treated with diuretics mainly HCT. However, similar study done in America to describe national anti-hypertensive medication indicated that CCBs and ACEIs were frequently prescribed for hypertensive patients[26]. In this study the reason for high proportion of diuretics use in hypertensive patients could be due to the fact that these drugs can also decrease cardio-vascular diseases and safe in patients who have heart failure and strokes[27]. Diuretics were also reported to be the mainly prescribed class of antihypertensive drugs in the United Kingdom[28] and Sub-Saharan countries[16] which is in agreement with the published international guidelines for antihypertensive treatment.

In many patients antihypertensive drugs were prescribed along with drugs having potential drug interaction. Most of antihypertensive drugs were prescribed along with NSAIDs which inhibit prostaglandin mediated vasodilatation and promote salt and water retention[29]. Diuretics, ACEIs, ARBs, BBs are likely to be more affected by NSAIDs than CCBs. Hence, switching to anti-hypertensive drugs not as susceptible to the blunting effect of NSAIDs should be considered for patients who are using chronic NSAIDs therapy. Alternative analgesics should be considered such as acetaminophen for patients requiring analgesics who are unable to have their anti-hypertensive regimen altered[29-31].

HCT and insulin were co-administered with antihypertensive drugs. Many clinicians hesitate to use diuretics, particularly, thiazide diuretics in patient with diabetes mellitus as they increase glucose concentration. The mechanism of diuretics induced hyperglycemia which may be related to drug induced hypoglycemia leading to decrease insulin secretion[32]. On other hand nine patients took a combination of antacids and captopril and it was found that patients' blood pressures were not improved after treatment. This could be due to the fact that antacids decrease bioavailability of captopril by delaying gastric empting and elevating gastric P_H[33].

CONCLUSION

Combination therapy was the most prescribed pattern to treat hypertensive patients in this study which is consistent with international guidelines. However, majority of patients in pre-hypertensive stage were treated by combination therapy which is not appropriate. Therefore, prescribers should consider when the combination drugs are to be used in hypertensive patients.

Some drugs were concomitantly taken with antihypertensive agents; among them NSAIDs were the most frequently prescribed drugs. Even

though NSAIDs and Insulin have a great role in patients with pain and diabetes mellitus, respectively, they have a potential to interact with antihypertensive agents. Hence, before prescribing and dispensing medication to hypertensive patients, the possible drug-drug interaction should be considered. In addition, physician and pharmacists should corporate to minimize drug interaction.

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