Use of Antihypertensive Medications in Patients with type -2 Diabetes in Ajman, UAE

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Abstract- Optimal reduction in blood pressure with antihypertensive agents helps to prevent microvascular and macrovascular complications of diabetes. The objective of the study was to evaluate the current utilization pattern of antihypertensive medications among patients with diabetes and coexistent hypertension as per the JNC seventh report guidelines. A Cross-sectional survey was conducted among patients with diabetes attending outpatient department of Internal Medicine at a hospital at Ajman. Medical records of patients were used to obtain diagnostic, demographic and drug use information. Univariate analysis was performed using *Chi*-square and t- test followed by logistic regression to compute independent predictors. Of 132 patients with diabetes, uncomplicated hypertension (HTN) was coexistent in 81% (107/132) of patients. Males constituted 49.5% (53/107) of the total. Mean (SD) age of patients with HTN was 55.1(10.1) years higher than those without HTN 49.6 (9.9) years (P<0.01). Higher number of patients with HTN had duration of diabetes < 5years than those >5 years (P=0.04). While adjusting the significant factors, only duration of diabetes was statistically significant (adjusted OR=1.06; CI 95% (1.003-1.116) P= 0.03 among patients with HTN. 63.6% (68/107) prescriptions contained one drug antihypertensive drug, 27.1 % (29/107) two drugs and 7.4% (8/107) no anti-hypertensive drug were prescribed. Angiotensin converting enzyme inhibitors/ Angiotensin receptor blockers (ACEI/ARBs) followed by diuretics were commonly prescribed drugs. ARBs with diuretics were the most frequent two drug combinations. The antihypertensive utilization pattern was similar in both gender and age groups. Results represent the current prescribing trend for anti-hypertensive agents among patients with diabetes that is in accordance with JNC-7 recommendations.

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Keywords: Anti-hypertensives; Diabetes; Drug utilization

Introduction

Diabetes Mellitus (DM) is one of the endocrine disorders, necessitating constant attention to diet, exercise, glucose monitoring, and medication to achieve good glycemic control. The prevalence of diabetes is on the rise with an estimated 350 million adults likely to acquire diabetes by 2030 (1). In United Arab Emirates (UAE), the prevalence of diabetes is about 20%, which is expected to reach 22% by 2025. In the prevalence rate is higher among the UAE citizens (25%) than in the expatriates (13–19%) (2).

DM is associated with a higher prevalence of risk factors such as hypertension (HTN) and dyslipidemia, which, in turn leads to major vascular complications (microvascular and macrovascular) (3). These complications are debilitating to the patient, and also associated with significant economic burden to the patient, family members, and the nation's health care budget. Al-Maskari *et al.,* from UAE documented a significant association between hypertension and presence of macrovascular disease among diabetic

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patients (4). About 35% of the patients with diabetes had coexistent hypertension. Optimal reduction in blood pressure with antihypertensive agents helps to prevent diabetic microvascular and macrovascular complications (5). With each year, the number of approved pharmacological treatment options for patients with hypertension is increasing. However, the choice of antihypertensive medication is influenced by many factors especially presence of co-morbid conditions. The seventh report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC) stated that angiotensin converting enzyme inhibitors/ Angiotensin receptor blockers (ACEI/ARB) is an important component of most regimens to control blood pressure in patients with diabetes (6).

The primary objective of the study was to evaluate and compare utilization of antihypertensive medications according to JNC 7th report for patients with diabetes.

Materials and Methods

This was a cross-sectional survey carried out among patients with diabetes attending outpatient department of Internal Medicine at a tertiary care hospital, Ajman over a period of three months from January to March 2011. The study was approved by the institutional ethics committee, and patient confidentiality was maintained. Participants were those with diabetes and uncomplicated hypertension, 18 years old and above attending the Internal Medicine during the study period. Medical records of patients were used to obtain diagnostic, demographic and drug use information. We reviewed all the case records of patients with diabetes and hypertension during the study period. Only one prescription was considered per patient. The data extracted from the medical records were transferred to a pilot tested structured questionnaire developed by the investigators. A total of six specialists in internal medicine were prescribing during the period of data collection. All data collected were analyzed using SPSS, version19.0 (Chicago IL, USA). Univariate analysis was performed using *Chi*-square and t- test followed by logistic regression to compute independent predictors. Multivariate analysis was further tested on variables found significant in Univariate analysis. *P*.value ≤0.05 was considered statistically significant.

Results

During the study period, a total of 132 prescriptions of patients with diabetes were monitored, of which 81% (107/132) had uncomplicated hypertension. Of the total 49.5%, (53/107) were males. The demographic and medical characteristics of 107 hypertensive patients with diabetes are presented in Table 1.

Table 1. Demographic characteristics of patients with and without hypertension among diabetics

Variable	Groups	HTN (n=107)	No HTN (n=25)	*P*. value
Age	**Mean age**	55.1±10.1	49.7±10.0	<0.01
Gender	**Male**	53 (49.5%)	10(40.0%)	0.39
	Female	54(50.5%)	15 (60.0%)	
Age group	**<45 years**	16 (15.0%)	9 (36.0%)	0.03
	45-60 years	55(51.4%)	12(48.0%)	
	>60 years	36(33.6%)	4(16.0%)	
Duration of DM	**<=5 years**	84(78.5%)	24(96.0%)	0.04
	>5 years	23(21.5%)	1 (4.0%)	

Of the 107 patients with HTN, 25 had co-existent dyslipidemia. A total of 30 patients had dyslipidemia (22.7%; 30/107). The mean (SD) age of patients with HTN was significantly higher than and those without HTN 55.1(10.1) years and 49.7(10) years, *P*<0.01. The mean (SD) age of males and females with HTN was similar, 53.2 (9.4) years and 54.9 (10.9) years. No gender differences were observed in patients with HTN and those without HTN. Based on the age groups, majority of the patients were in the age group of 45-60 years compared to other age groups. The difference in proportion was statistically significant (*P*=0.03). Significantly higher number of patients with HTN had duration of diabetes <5 years (*P*=0.04). To find the degree of association between mean age of the patient and the duration of diabetes and the occurrence of DM simple binary logistic regression was applied. It was found that with unit increase in the age (one year) 6% increase in the risk to develop HTN which was statistically significant (Odds ratio (OR)=1.06; C.I95% (1.01-1.11)) (*P*=0.02). With respect to the duration of diabetes, if the duration of diabetes is more than five

years there is six times more chance to develop HTN (OR:6.5 CI95%:0.84-51.19, *P*=0.07).

To eliminate the effect of confounding variables, multiple logistic regression was applied and the results showed that the adjusted OR for duration of DM was not statistically significant, but the adjusted OR for the age was 1.06; CI: 1.003-1.116, p= 0.03) which is statistically significant. Thus, it can be concluded that the only factor associated with the occurrence of HTN is the age of the patient.

Of the total, single antihypertensive drug was found in 63.6% (68/107) of the prescriptions, two drug combinations in 27.1 %(29/107) of prescriptions, two prescriptions contained three-drug combinations and 7.4% (8/107) patients did not receive any drug. ARBs were the most commonly prescribed antihypertensive medications and ARBs with diuretics were the most frequent two drug combinations. Among the diuretics, thiazide diuretics were the most frequently prescribed. The overall utilization of individual drug classes, as monotherapy and combination therapy, is shown in tables 2 and 3.

The utilization pattern of most common antihypertensive medication based on gender, age groups and duration of DM is listed in table 4. Statistical significance was not noted in the utilization pattern of common antihypertensive medications (monotherapy and combination therapy) with regards to gender, age groups and duration of DM.

Table 2. Antihypertensive medications in monotherapy and combination therapy

Drug class	Monotherapy	Combination therapy	Overall utilization
ACEI/ARBs	42	25	67
Beta blockers	19	2	21
Calcium channel blockers	7	7	14
Diuretics	-	23	23

Table 3. Monotherapy versus Combination therapy of antihypertensive medications

Type of treatment	Drug classes	Number	Percentage
Monotherapy	ACEI/ARBs	42	39.2
	Beta blockers	19	17.7
	Calcium channel blockers	7	6.5
Two-drug combination	ACEI/ARBs +Diuretics	22	20.5
	ACEI/ARBs + Calcium channel blockers	5	4.6
	Calcium channel blockers + Beta blockers	1	0.9
	ACEI/ARBs + Beta blockers	1	0.9
Three drug combination	ACEI/ARBs+ Diuretics + Calcium channel blockers	2	1.8

Table 4.Utilization of the most common antihypertensive medications based on gender, age groups and duration of DM

Variable	Groups	ACEI/ARBs (n=42)	Beta Blockers (n=19)	ACEI/ARBs+ Diuretics (n=22)
Gender	**Male**	18	12	11
	Female	25	7	11
Age group	**<45 years**	5	4	2
	45-60 years	20	10	11
	>60 years	18	5	9
Duration of DM	**<5 years**	32	13	18
	>5 years	11	6	4

Discussion

The risk of macrovascular and microvascular events in patients with diabetes and hypertension is significantly high, and the optimal control of blood pressure can significantly lower the increased risk of cardiovascular events. We evaluated the patterns of antihypertensive drug therapy in diabetic hypertensive patients. This study showed that nearly 80% of the patients had a co-existing hypertension. Maskari *et al*., findings from UAE reported 35% of patients with diabetes had a co-existing hypertension (4).

Current study revealed that about 63.6% patients were on single antihypertensive therapy and 27% on combination therapy. Use of multiple drugs in combinations is being increasingly recognized as critical to control hypertension in patients with diabetes. Johnson *et al.*, reported that 70% of the patients with HTN among diabetics were on multidrug regimen (7).

The commonest drug class prescribed was ACEI/ARBs similar to previous reports (7,8), and this pattern of utilization is a per the JNC VII recommendation for patients with HTN and diabetes (6). These findings indicate that medication use was mostly consistent with JNC 7th report recommendation among diabetic hypertensive patients. ACEI/ARBs were the most commonly prescribed drug classes both in monotherapy and combination therapy. The use of ACEI/ARBs among diabetic hypertensive patients is in accordance with the JNC recommendations for the management of hypertension among diabetic hypertensive patients. ACEI and ARBs are the preferred antihypertensive medication for the management of hypertension among diabetic hypertensive patients. The reported monotherapy and combination therapy use of ACEI/ARBs were 39.2% that is consistent with reports from Palestine and Bahrain (8,9). Evidence from the HOPE trial (The heart outcomes prevention evaluation study) suggested the cardiovascular protection benefits of ACEI in hypertension (10). ACEIs /ARBs produce antihypertensive effect by reducing the levels of angiotensin II/ blocking angiotensin II Type I receptors leading to vasodilatation and fall in blood pressure, it also reduces the harmful effects of angiotensin II on the cardiovascular and renovascular system.

Beta-blockers accounted for 17.7% of the drugs when considering monotherapy of antihypertensive drug class, while Sweileh *et al.*, reported diuretics were second most common antihypertensive drug class (8). Cardioselective blockers with vasodilating action (α-blockers) are preferred to minimize metabolic interference in these patients.

Diuretics were ranked second when considering the overall utilization of antihypertensive drugs. Combination of ACEI/ARB with a thiazide diuretic was the most commonly prescribed. Diuretics offer both cardiovascular and renal protection does not increase risk for diabetes, and their safety and beneficial effects in this population are well established. JNC VI recommended them as one of the preferred therapies in this population. This utilization was consistent with evidence based practice guidelines (11). This combination is pharmacologically favorable since it produces an additive antihypertensive effect, balances out the diuretic-induced increase in plasma renin activity, and minimizes metabolic effects of thiazide diuretics like hypokalemia and hyperglycemia (12). Several clinical trials (ALLHAT, ADVANCE) have highlighted the anti-hypertensive effectiveness of this combination in hypertension (13-15).

The strength of the present study is assessment of the actual prescriptions dispensedto the patients. The limitations of the study include the small sample size included and the findings from a single center which restricts the generalization of the findings. However, future longitudinal surveillance on utilization of antihypertensive medications among patients with diabetes can be performed based on the results from these studies and practices between institutions, regions and countries can be compared to rationalize prescribing practices.

In conclusion, findings showed ACEI/ARB use in a large proportion of diabetic hypertensive patients which represent the current prescribing trend for anti-hypertensive agents among patients with diabetes in accordance with evidence- based practice guidelines (JNC-7 recommendations). The observations of this study provide a framework for continuous prescription audit to create a database on antihypertensive medication prescribing patterns among patients with diabetes.

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