Target Blood Pressure Attainment in Diabetic Hypertensive Patients: Need for more Diuretics?

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Abstract

Objective: To determine target blood pressure attainment and to evaluate blood pressure control relative to type of therapy among diabetic hypertensive patients. **Methodology**: An observational retrospective study of all diabetic hypertensive patients visiting Al-Watani governmental medical center from August 01, 2006 until August 01, 2007. The blood pressure (BP) measurement made during the patient's recent visit and documented in the medical files was used in the study. Controlled BP values for hypertensive patients with diabetes mellitus were defined per JNC 7 guidelines: 130/80 mm Hg or lower. Proportions of use of 5 different antihypertensive drug classes were compared between patients with controlled and uncontrolled BP. **Results**: Of the 311 patients, 79 (25.4%) had their BP controlled. No significant differences in age, gender, body weight, duration of hypertension or diabetes, renal function, average number of anti-hypertensive medications and doses of most commonly reported antihypertensive medications were found between controlled and uncontrolled BP groups. ACE-I/ARB was the most commonly used drug class in both groups. Overall, the use of ACE-I/ARB, beta blockers, calcium channel blockers, alpha-blockers and multi drug regimens were also not significantly different between the controlled and uncontrolled groups. However, overall use of diuretics was significantly higher in controlled group than uncontrolled group (59.5% versus 45.7%, $P < 0.001$). **Conclusion**: Despite the common use of ACE-I/ARB as recommended per JNC 7th report, the majority of the patients had uncontrolled BP. Diuretics is an important drug class in attaining target BP. Use of diuretics in combination with ACE-I as well as drug compliance needs to be emphasized and encouraged.

Key words: Hypertension, Diabetes mellitus, JNC 7, Target Blood Pressure.

1. **Introduction**

The major adverse outcomes of diabetes mellitus are a result of vascular complications, both, at the microvascular (retinopathy, nephropathy or neuropathy) and macrovascular levels (coronary artery disease, cerebrovascular and peripheral vascular disease). These vascular complications are augmented by the co-existence of hypertension [1]. The seventh report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) and the American Diabetes Association (ADA) recommended that blood pressure (BP) in diabetics be controlled to levels of 130/80 mm Hg or lower [2, 3]. The JNC 7 stated that angiotensin converting enzyme inhibitors (ACE-I) is an important component of most regimens to control BP in diabetic patients. In those patients, ACE-I may be used alone, but much more effective when combined with thiazide-type diuretic or other antihypertensive drugs.

This study aimed to assess the attainment of target BP as recommended by the JNC 7th report and ADA recommendations and to compare the anti-hypertensive use among patients attaining the target BP versus those who do not.

2. Methodology

2.1 Settings

We conducted this study at Al-Watani governmental hospital and medical center, the largest non-surgical medical center in north Palestine with in and out-patient community medical services. Practitioners at this center were a combination of specialized and general physicians. All aspects of the study protocol, including access to and use of the patient clinical information, were authorized by the university medical ethics committee and the health authorities.

2.2 Blood Pressure Definition and Measurement

In this study, target (controlled) BP was defined as 130/80 mmHg or lower according to the JNC 7th report. Blood pressures higher than the target BP were termed uncontrolled BP. In the medical center where the study was carried out, BP measurement is done routinely by the trained nurse or physician and documented for most patients attending the center.

2.3 Participants and Study Design

All patients with documented diagnosis of diabetes mellitus and hypertension and seen from August 1, 2006 to August 1, 2007 were investigated. We performed a retrospective analysis of data obtained from medical files of those patients. Data abstracted included demographic information, clinical history, vital signs, and anti-hypertensive drug therapy used in the past six months. BP value measured at the most recent visit of the patient to the medical center was abstracted and used in further classification of patients (controlled versus uncontrolled). Patients with missing data regarding their most recent BP values or medications and those on renal dialysis were excluded.

2.4 Antihypertensive Drug Therapy

Antihypertensive drug classes (β-blockers, calcium channel blockers, thiazide/ loop diuretics, ACE-I/ ARB, and α-blockers) were recorded. ACE-I and ARB were grouped together because of the very few patients using ARB. Thiazide and loop diuretics were grouped together under "diuretics". The number of antihypertensive drugs being prescribed was tabulated. We classified patients with any prescriptions for ACEI or ARB as ACEI/ARB users. The proportion of use of these antihypertensive drug classes, among patients with controlled and uncontrolled BP was tabulated then we compared the proportions of drug class use among patients with and without controlled BP.

2.5. Outcome of Interest

Using the clinical data collected, we determined the BP goal attainment by comparing the patient's most recent BP reading documented in the patient's medical file during his current visit with the BP goal stated in the JNC 7^{th} report. Further, we compared the clinical profile of patients who attained the goal BP with those who did not.

2.6 Statistical Analysis

Independent samples t-test and Chi square test, whatever appropriate, were used to test significance between variables of the two groups. Data were expressed as mean ± SD for continuous variables and as frequency for categorical variables.

3. Result

A total 358 patients were investigated during the study period. Forty seven patients were excluded (32 were on renal dialysis and 15 patients had missing clinical data). Therefore, 311 diabetic hypertensive patients were included in the analysis. Seventy nine (25.4%) of the patients had their blood pressure at the target level of (Controlled BP group) and the remaining 232 (74.6%) of the patients were not at the target BP (Uncontrolled BP group). Table 1 differentiates between patients with controlled BP and those who were not. No significant differences were found between controlled and uncontrolled BP groups in age, gender distribution, body weight, renal function, duration of either hypertension or DM, and average number of anti-hypertensive medications receiving. However, the controlled group significantly had lower SBP and DBP than the uncontrolled BP group.

Of the 79 patients who were in the controlled BP group, 7 (8.9%) patients were on no drug therapy, 27 (34.2%) were on one, and 45 (56.9%) were on ≥ 2 drugs. Of the 232 patients who were in the uncontrolled BP group, 23 (10%) were on no drug therapy, 97 (41.8%) were on one, and 112 (48.3%) were on ≥ 2 drugs. The differences in the use mono and combination therapy between the two groups were not significant. Overall, BP control was 25.4%: 23.3% among untreated patients, 21.8% among patients on monotherapy, and 28.7% in patients receiving multidrug regimens. None of these proportions were statistically significant from each other (mono versus multidrug regimen, $P = 0.21$).

Pattern of use of anti-hypertensive medications in the controlled and uncontrolled BP groups is shown in table 2. Use of all drug classes, except for diuretic class, was not significantly different between the two groups. Use of diuretics drug class was significantly higher among patients in the controlled BP group compared to those in the uncontrolled BP group (59.5% versus 45.7%, $P < 0.001$). It is noteworthy that the overall use of ACE-I/ ARB and diuretics drug classes in the controlled BP group was similar (60.8% versus 59.5%). The most commonly used drug combination in the controlled group was ACE-I/ diuretic which was used in 19 (24.1%) patients. The overall use of ACE-I/ ARB (63.4%) and diuretics (45.7%) drug classes in uncontrolled BP group were different with diuretics being less used than ACE-I. The most commonly used drug combination in the uncontrolled BP group was also ACE-I/ diuretic which was used in 50 (21.6%) patients. The difference between the controlled and uncontrolled groups in the use of ACE-I/ diuretic was not significant (P = 0.82).

No significant differences were observed when the doses of most commonly used antihypertensive drugs used in both controlled and uncontrolled BP were compared. Enalapril, the most commonly used type of ACE-I, was used with an average dose 16 ± 12.5 mg/ day among the controlled BP group compared with 18.6 ± 12.4 mg/ day in the uncontrolled BP group (P = 0.25). Furosemide, the most commonly used type of diuretic, was used with an average of 66.6 ± 37.7 mg/ day in the controlled BP group compared with 65.4 ± 40 mg/ day in the uncontrolled BP group (P = 0.89).

4. Discussion

In this study, we investigated the attainment of target blood pressure as defined by JNC 7th report in this high risk category of patients. There were approximately 25% of the patients with controlled blood pressure, a slightly lower than that reported by Andros and co-workers (28%), higher than that reported by Mori and co-workers (11.3%), Sequeira and co-workers (10%) and Singh and co-workers (11.2%) [4-7]. In this study, more than 60% of the patients in both controlled and uncontrolled BP groups were using ACE-I/ ARB and approximately half of the patients in both groups were on combination therapy. This is in accordance with JNC 7th report recommendation.

One might argue that the most recent blood pressure values measured at the medical canter and used in this study might not truly represent the blood pressure of the patients at home. However, a previously published study has used one BP reading abstracted from patient's medical files to categorize patients into controlled and uncontrolled BP groups [4]. Furthermore, the same study has found that using one BP reading versus using an average of three previous BP reading did not make a significant difference in the proportion of controlled BP patients (27.6% when one BP value is considered versus 30% when three BP values were considered) [4].

It was interesting to note that the extent of BP control achieved in groups treated with mono-therapy versus multidrug therapy did not differ significantly. Similar findings were obtained by Sequeira and co-workers and Westheim and co-workers [6, 8]. Several potential explanations could be proposed for the high proportions of poor BP control and for the lack of difference in BP control among patients on mono versus multidrug versus those on no pharmacological therapy. First, it could be due to lack of drug compliance among diabetic patients as a result of adverse events of the anti-hypertensive medications. It has been reported by several studies that drug compliance among hypertensive patients is relatively low [9]. A study has found that antihypertensive drugs were used regularly by only 62% of hypertension patients, with forgetting and feeling of well-being without therapy the principal reasons given for irregular drug taking. Hypertensive patients who were aware that increased BP reduces life span used the prescribed drugs more regularly and came regularly for checkups compared with patients lacking the relevant information. Patients over 60 years of age and smokers exhibited the worst compliance [9]. A study carried out by the author at the same medical center and on diabetic hypertensive patients five years ago have shown that approximately 42% of the patients investigated had good compliance on antihypertensive medications [10]. A second potential explanation for the low proportions of controlled BP and which could be interpreted from the results is the relatively lower diuretic use among patients with uncontrolled BP compared to those with controlled BP group. A third, yet a weaker explanation, is the less aggressive anti-hypertensive therapy among the uncontrolled group compared to the controlled group.

In this study, it was also noted that 7 (8.9%) patients in the controlled BP group were on no pharmacological therapy. This might be surprising and difficult to explain. However, it is possible that those patients have been recently diagnosed with hypertension and were controlled with non-pharmacological therapy and therefore on drug treatment was yet initiated. Furthermore, the use of retrospective chart review to identify medications is sometimes un-reliable since this documentation is likely to be inconsistent, incomplete and inaccurate. The lack of any pharmacological therapy in 23 (10%) patients in the uncontrolled BP group, however, might be the possible reason why those patients were having uncontrolled BP.

The use of diuretics among diabetic hypertensive patients may have unfavorable effects on lipid profile, glucose homeostasis, electrolytes and serum uric acid. However, thiazde-type diuretics are known to be beneficial in diabetics and are generally well tolerated [11,12]. In the pre-specified diabetic subgroup of ALLHAT, therapy that began with chlorthalidone reduced the primary end point of coronary heart disease and myocardial infarction to the same degree as therapy based on lisinopril or amlodipine [12]. JNC 7 indicated that although ACE-I may be used alone for BP lowering in diabetic patients, they are much more effective when combined with a thiazide-type diuretics or other antihypertensive drugs.

5. Limitations

The conclusions made from this study can not be conclusive given the following limitations of the study: (1) this is a single centre, retrospective study on relatively small sample (n=311) of patients with diabetes mellitus and hypertension; (2) no information were available to the author regarding compliance of the patients on the antihypertensive medications prescribed for both controlled and uncontrolled groups and finally (3) the retrospective nature of the study.

6. Conclusion and Recommendation

Despite of the limitations mentioned above, this study concluded that diabetic hypertensive patients mostly had uncontrolled BP as defined by JNC 7 despite their use of recommended drug classes and regimens. Underutilization of diuretics or poor drug compliance might be a potential cause of uncontrolled BP in this category of patients. Further multicenter studies with larger number of patients and blood pressure follow up is recommended to explore the role of diuretics as well as other factors like drug compliance in the attainment of goal Bp among this category of patients.

7. References

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Table 1. Characteristics of patients in controlled and uncontrolled BP groups.

Characteristic	Controlled BP N = 79	Uncontrolled BP N = 232	P
Age (years)	66.3 ± 11.11	64.3± 10.86	NS
Gender (Male)	35 (44.3%)	99 (42.7%)	NS
Duration of HTN (years)	5.9 ± 6.1	7.7 ± 7.8	NS
Duration of DM (years)	9.9 ± 7	12.3 ± 9.2	NS
CHF	22.8%	16.4%	NS
CrCl (ml/min)	87.5 ± 52.7	100.5 ± 75.8	NS
Body Weight (kg)	74.6 ± 13.4	74.5 ± 13.2	NS
RBG (mg/dL)	264.4 ± 141.5	259.5 ± 129	NS
SBP (mmHg)	118.7 ± 10.4	160.6 ± 24.8	< 0.001
DBP (mmHg)	73.7 ± 6.86	101 ± 28.3	< 0.001
Number of anti-hypertensive medications	1.6 ± 0.8	1.5 ± 0.8	NS

CHF: congestive heart failure. CrCl: creatinine clearance, RBG: random blood glucose

NS: not significant.

Table 2. Patterns of use of anti-hypertensive medications among patients in the controlled and uncontrolled BP groups.

No. of Patients N (%) Drug Class	**Among Patients with Controlled BP[1]** 79 (25.4%)			**Among Patients with Un-controlled BP[2]** 232 (74.6%)		
	Overall 79 (100)	**1 Drug** 27 (34.2)	**≥ 2 Drugs** 45 (56.9)	**Overall** 232 (100)	**1 Drug** 97 (41.8)	**≥ 2 Drugs** 112 (48.3)
ACE-I/ ARB	48 (60.8)	14 (51.9)	34 (75.6)	147 (63.4)	57 (58.8)	90 (80.4)
Thiazide or loop diuretics	47 (59.5)*	9 (33.3)	38 (84.4)	106 (45.7)	24 (24.7)	82 (73.2)
Calcium channel blockers	18 (22.9)	2 (7.4)	16 (35.6)	60 (25.9)	9 (9.3)	51 (45.5)
B-blockers	12 (15.2)	2 (7.4)	10 (22.2)	22 (9.5)	7 (7.2)	15 (13.4)
Alpha blockers	1 (1.3)	0 (0)	1 (2.2)	5 (2.2)	0 (0)	5 (4.5)

Note: Percentages of individual drug classes are given within columns; overall, and by number of drugs in regimen.

[1] Controlled BP group: 7 (8.9%) patients were on no drug therapy.

[2] Uncontrolled: 23 (10%) were on no drug therapy.

*Significantly higher than the overall diuretic use in uncontrolled BP group.