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The Management and Treatment of Hypertension in Patients with Diabetes

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## PERMISSION

Title: The Management and Treatment of Hypertension in Patients with Diabetes.

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### **Abstract**

Today, the combination of diabetes mellitus (DM), either Type 1 or Type 2, and hypertension (HTN) have led to an increase in micro and macro vascular damage resulting in enhanced development of cardiovascular disease, cerebral infarction, nephropathy, neuropathy, and retinopathy. Prolonged HTN in patients with diabetes results in irreversible damage to the blood vessels which leads to early formation of atherosclerotic plaques that can dislodge causing a thromboembolic event. Tight control of blood pressure in patients with diabetes is required to prevent vascular remodeling; however, there remains some confusion regarding appropriate blood pressure parameters in patients with diabetes. Per the American Diabetes Association (ADA) 2017 Guidelines and Joint National Commission 2017 Hypertension Guidelines, the recommended goal blood pressure in patients with diabetes is a systolic blood pressure (SBP) less than 140 mm Hg and diastolic blood pressure (DBP) less than 90 mm Hg. However, depending on the person's health history, comorbidities, and risk factors, more stringent control may need to be considered. Ultimately, with a blood pressure greater than 140/90, initiation of a pharmacological agent is required. However, the ideal antihypertensive agent to initiate remains challenging for clinicians and requires use of evidence-based data combined with patient risk factors to determine the best course of action. Therefore, setting appropriate parameters for blood pressure control, as well as selecting the appropriate treatment modality, is a primary goal of the primary care provider to manage and treat hypertension in patients with diabetes.

*Keywords:* diabetes, hypertension, management

## The Management and Treatment of Hypertension in Patients with Diabetes

### **Background**

A pleasant 60-year-old female presented to the clinic for management and treatment of diabetes. She reported being diagnosed about two years ago and had been taking metformin twice a day. In addition to diabetes, she has a past medical history of hypertension and hyperlipidemia. Her last clinic visit was over a year ago and today she had elevated cholesterol and glycosylated hemoglobin (Hgb A1C) levels, as well as high blood pressure. Based on the data collected and the medical history, the patient was at risk for complications associated with hypertension and requires interventions, either pharmacological or non-pharmacological to control.

In the patient with diabetes, elevated blood pressure can result in life threatening complications such as the development of microvascular and macro vascular disease. Quick identification and treatment of hypertension is crucial to maintaining health and wellness, especially in patients with diabetes, wherein tighter blood pressure control is required to prevent health risks. Already, the prevalence of hypertension in patients with diabetes today continues to result in substantial morbidity and mortality (Vijan, & Hayward, 2003). Therefore, understanding the risks and knowing the proper treatment course will prevent life altering conditions and promote quality of life.

The parameters for blood pressure control in patients with diabetes has been widely researched and, per the American Diabetes Association 2017 Guidelines and Joint National Commission 8 Guidelines, the goal for patients with diabetes is a systolic blood pressure is less than 140 and a diastolic blood pressure less than 90. However, after reviewing the literature, there is still some debate on the optimal blood pressure to minimize diabetic complications and

maintain quality of life. Furthermore, treatment of hypertension in patients with diabetes is also challenging due in part to conflicting evidence about appropriate drug regimens; combined with genetic, environmental, and psychosocial factors the struggle to control increases. The use of antihypertensive are reserved for patients with diabetes whose blood pressure remains elevated despite lifestyle modifications. Therefore, understanding the parameters for blood pressure control in patients with diabetes and how best to treat them will minimize the risk of vascular complications that can result in end organ damage.

### **Case Report**

A pleasant 60-year-old female in no acute distress was seen in clinic for management of her diabetes. She had a medical history of diabetes mellitus with lower extremity neuropathy, hypertension, hyperlipidemia, and a past family history of coronary artery disease (CAD) and colon cancer. She had a drug allergy to penicillin. Her home medication list consisted of daily Aspirin 81 mg, Atorvastatin 20 mg, Lisinopril 20 mg, Multivitamin, and Metformin 500 mg two times a day (BID). She denied history or current tobacco abuse or illicit drug use. She was a social drinker, but denied history of abuse. She had received her influenza and shingles vaccination. Her health maintenance screenings were up to date apart from a colonoscopy and DEXA scan.

In review of her systems, the patient denied any acute illness or changes to her health. Patient was alert and able to answer questions appropriately. She denied fevers, chills, dizziness, or syncopal episodes. She denied respiratory alterations such as shortness of breath or dyspnea. She denied cough with or without sputum production. She denied cardiac dysfunction such as acute chest pain, cardiac palpitations or peripheral edema. Her bowel and bladder patterns remain unchanged. She denied heartburn or GI distress. She reported no abdominal pain or

discomfort. She denied altered musculoskeletal function or difficulty with mobility. She denied joint pain, back pain, or muscle pain. She reported good nutritional intake on a regular diet.

A thorough physical examination was conducted on the patient. Initially, her vital signs were as follows: blood pressure 148/98, heart rate 80, respiratory rate 20, and temperature 98.6 degrees Fahrenheit. In general, the patient was a well-developed female in no acute distress with good mentation and affect. Her head was normocephalic, ears bilaterally set with no alterations in hearing, vision intact with good ocular movement noted, and her neck and throat were symmetrical with no thyromegaly present. An assessment of her lungs resulted in good inspiratory and expiratory capacity, symmetrical lung expansion, and no signs of respiratory distress. On auscultation her lungs were clear bilaterally within all lobes. Her cardiac assessment revealed regular rhythm and rate with good S1 and S2 heard, no murmurs, clicks or rubs. Peripheral pulses were 2+ and palpable with signs of adequate circulation as evidenced by no peripheral edema. Abdomen was soft and nontender to palpation and active bowel sounds in all four quadrants. Skin was dry, but intact with no evidence of slow healing ulcers or wounds. Patient exhibited no difficulty with mobility or movement of all extremities. Microfilament testing revealed evidence of neuropathy on bilateral feet. Neurologically the patient had all cranial nerves II-XII intact.

A crucial element of the patient's assessment is to obtain laboratory tests that will aid the clinician in creating a treatment plan that is best suited for the patient. Laboratory testing required and completed was a basic metabolic panel, Hgb A1C, and lipid panel. A BMP will measure her electrolytes and renal function; which was found to be within defined limits apart from an increased glucose at 138 and decreased eGFR at 53. Obtaining an Hgb A1C is important to understand the patients average blood glucose levels in the last 3 months. Her Hgb A1C was

elevated at 7.8%, indicating an average blood glucose of 177 (Diabetes Care, 2008). Lastly, the patient required a cholesterol or lipid panel to identify her propensity for developing atherosclerosis leading to CVD. Her lipid panel revealed elevated triglycerides at 186 mg/dL and an elevated total cholesterol of 220 mg/dL.

Based on the medical history, physical examination, and review of laboratory results, the impression and plan for this patient should focus on lowering blood pressure, cholesterol, and blood sugars. Per the ADA 2017 Guidelines, the goals for this patient should include a BP less than 140/90, triglyceride level less than 150 with a total cholesterol level less than 199, and Hgb A1C less than 6.5. However due to the family history of cardiovascular disease and her risk for developing kidney disease, consider a BP goal less than 130/80 (Boer, et al., 2017). Her plan would require an increase in Lisinopril to 40 mg daily, increase Atorvastatin to 40 mg daily, and increase Metformin to 1000 mg BID. In addition to pharmacological interventions, the patient requires education regarding management of diabetes. Currently the patient reported that her lifestyle includes limited physical exertion and irregular eating habits. Education about lifestyle modifications should include addition of daily exercise, maintaining a healthy BMI, and moderating nutritional intake.

In addition to increasing her medication dosages and modifying her daily habits, the patient needs referrals to appropriate clinicians that can monitor her disease progression and prevent organ damage. Thus, scheduled appointments with a nephrologist and ophthalmologist are required. Plan to repeat labs in 3 months to monitor her lipid levels, electrolytes and kidney function, and Hgb A1C. In addition to ordering repeat laboratory testing and specialty referrals, the patient should be educated on checking her blood sugar levels and blood pressure daily to identify trends and treat accordingly.



### **Literature Review**

Hypertension is common among patients with diabetes, with the prevalence depending on the type and duration of diabetes, age, sex, race/ethnicity, BMI, history of glycemic control, and the presence of kidney disease, among other factors (Boer, et al., 2017). The evidence suggests that more aggressive control of blood pressure is preferred in patients with diabetes than without to decrease the risk of atherosclerotic cardiovascular disease, microvascular and macro vascular complications. Initially and at every clinic visit, blood pressure readings need to be obtained to detect trends of elevated blood pressure. For a patient to be identified as having high blood pressure, they require an elevated reading on a separate day within one month of initial reading (Boer, et al., 2017). However, interpreting blood pressure readings and understanding the risks it can pose on the patient's health is crucial. There is no exact blood pressure measurement in patients with diabetes that will prevent complications, however, several research studies have been conducted to determine the appropriate blood pressure levels to minimize health risks.

Per the American Diabetes Association 2017 Guidelines, the goal blood pressure is a systolic blood pressure less than 140 and a diastolic blood pressure less than 90 (Boer, et al., 2017), which coincides with Joint National Committee 8 recommendations. In a non-complicated patient with diabetes with minimal comorbidities and risk factors, this would be an ideal goal that could be obtained with lifestyle modifications. Often, this goal is set for adults aged 30-59 whose risks for developing complications is minimal. An online medical database known as Up to Date, which is beneficial in assisting healthcare professionals to obtain current evidence-based health information on various health topics recommends in all patients with diabetes a blood pressure less than 140/90 (Bakris, 2017). It is important to remember that early

identification and treatment of hypertension in patients with diabetes is required no matter their age to prevent micro or macro vascular complications.

Lower blood pressure parameters are indicated for people who have renal or cardiac dysfunction. Per the National Kidney Foundation and the 2017 American Cardiology/American Heart Association hypertension guidelines, the recommended blood pressure should be less than 130/80 mm Hg, with an optimal target below 120/80 mm Hg in people with diabetes (Konzem, Devore, & Bauer, 2002; Bakris, 2017). Hypertension is often present in patients with type 2 diabetes that can lead to renal disease, which is suspected with the presence of micro and macro albumin in the urine. The presence of micro albuminuria can result in accelerated renal dysfunction and eventual failure within the diabetic population. Therefore, based on the blood pressure recommendation above, to prevent the occurrence of renal complications in patients with diabetes, a lower blood pressure is indicated and should be obtained with pharmacologic therapy.

As mentioned, a stricter blood pressure parameter is indicated to prevent cardiovascular complications. A meta-analysis was completed and found that a BP less than 130/80 resulted in less atherosclerotic cardiovascular disease (ASCVD) events, myocardial infarctions, and strokes (Franklin & Wong, 2017). Due to the results of the meta-analysis, they concluded all people with or without cardiovascular disease should aim for a BP less than 130/80. However, the clinician must consider that blood pressure is multifactorial and lower measurements may result in additional adverse effects especially within the elderly population. Clinicians should aim for these measurements, but treatment in lowering should be conducted safely with consideration of the patient and their health needs.

It is safe to conclude that lower blood pressure greatly decreases complications in patients with diabetes, however can blood pressure less than 120/80 be more damaging than beneficial in patients with diabetes? Epidemiological evidence demonstrates that BP less than 120/80 is associated with increased cardiovascular events and mortality in patients with diabetes (Arauz-Pacheco, Parrott, & Raskin, 2002). The ACCORD trial examined the effects of intensive blood pressure control less than 120/80 and concluded that there was no reduction in the rate of fatal and nonfatal major cardiovascular events (Cushman, et al., 2010). However, lower blood pressure did result in volume depletion leading to orthostatic changes, increased syncopal episodes, and kidney injuries due to lack of adequate perfusion. As many of the symptoms of volume depletion and hypoglycemia are similar, it can be challenging for the patient to understand the cause of their symptoms, resulting in greater caloric intake due to concern of hypoglycemia. Therefore, treatment strategies to control blood pressure in patients with diabetes need to be monitored closely for the development of adverse effects that can worsen glycemic control.

Treatment strategies to control blood pressure requires the use of antihypertensive medications known as angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), diuretics, calcium channel blockers, and beta adrenergic blockers. In choosing an antihypertensive agent, consider agents that will prevent mortality, prevent adverse cardiovascular events, and prevent the development and progression of renal disease (Bakris, 2017). There can be adverse drug reactions associated with antihypertensive, therefore caution is warranted when prescribing these drugs and should be chosen based on an individual's health history and risk factors.

Initiating anti-hypertensive therapy on a person with diabetes begins with an ACE-inhibitor. ACE-inhibitors block the conversion of angiotensin-I to angiotensin-II both systemically and locally in multiple tissues as well as plasma (Aronow et al., 2011). The result is relaxed blood vessels resulting in lower blood pressure and greater reabsorption of water by the kidneys. Its primary benefit in the control of blood pressure in patients with diabetes is to prevent the progression of diabetic renal disease and reduction in CVD outcomes. In addition to efficacy, these agents have the additional advantage of being particularly well tolerated since they produce few idiosyncratic side effects and do not have the adverse effects on lipid and glucose metabolism seen with higher doses of diuretics or beta blockers (Townsend, 2017). Some adverse effects of this drug class are hypotension, reduction in GFR, hyperkalemia, anemia, angioedema, or cough being the most common. Overall, this drug class is well tolerated and used as first line treatment of HTN in patients with diabetes.

Another antihypertensive drug class that is arguably equal as a first line agent in lowering blood pressure are angiotensin II receptor blockers (ARB). This drug class plays a role in protecting the kidneys in type 2 diabetes mellitus, both in established diabetic nephropathy with proteinuria and in patients with micro albuminuria (Aronow et al, 2011). This is the preferred initial drug class in patients with heart failure, hypertension, and diabetes per the ADA 2017 guidelines as they are capable of reducing mortality. The adverse effects of this drug class are similar to ACEI such as angioedema, hypotension, and cough as the most common symptom.

Both ACEI and ARBs effect the renin-angiotensin system, which controls blood pressure through management of blood volume and pressure (Singh, Mensah, & Bakris, 2010). Several studies have been conducted that found taking both an ACE-inhibitor and an ARB can lead to worse renal function resulting in development of diabetic nephropathy and chronic kidney

disease. The use of combined antihypertensive therapy is often needed to control blood pressure; however, it is not recommended that both an ACEI and an ARB be used together due to risk of CV events.

Diuretics are also utilized in the management and control of hypertension in patients with diabetes. Diuretics reduce total body sodium through their natriuretic action and have been shown to have vasodilatory effects (Arauz-Pacheco, Parrott, and Raskin, 2002). They primarily act on the renal system and can result in electrolyte imbalances that can alter cardiac function, resulting in the development of life threatening arrhythmias. They can also cause increased insulin sensitivity in patients with diabetes, resulting in better glycemic control. Their use is indicated in people with CAD, congestive heart failure, diabetes, and hypertension. The use of diuretics as a monotherapy is acceptable in the treatment of heart failure, however for control of blood pressure in patients with diabetes combined therapy with a beta blocker is preferred, especially to halt or hinder deterioration of renal function.

The use of calcium channel blockers has gained favor in the treatment of HTN in patients with diabetes. They inhibit calcium influx through membrane-bound voltage dependent calcium channels, resulting in decreased intracellular calcium levels and vasodilation (Arauz-Pacheco, Parrott, and Raskin, 2002). They can be divided into 2 classes: dihydropyridine and nondihydropyridine. The dihydropyridine CCBs (e.g., nifedipine and amlodipine) are more selective in blocking L-type calcium channels in vascular smooth muscle cells, inducing vascular relaxation and reduced BP, compared to nondihydropyridine CCBs (e.g., diltiazem and verapamil) (Aksnes, Skarn & Kjeldson, 2018). They have a great impact on preventing cardiovascular events by altering lipid and carbohydrate metabolism. In one study, the use of CCB resulted in increased risk of diabetic nephropathy due to the increase in proteinuria.

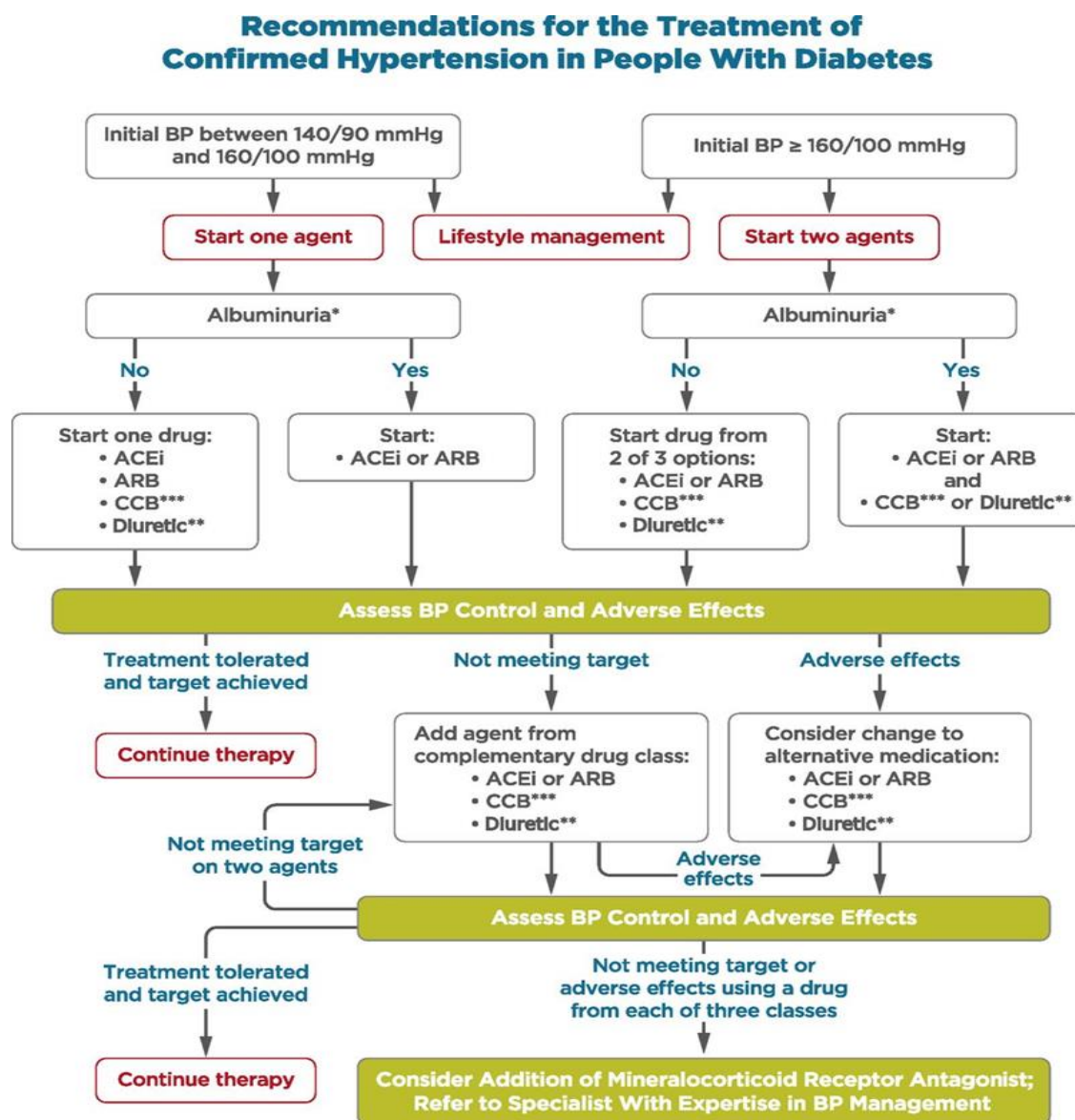
Therefore, the recommendation is combining a CCB with an ACE inhibitor or an ARB to prevent renal dysfunction. Overall, CCBs are well tolerated and very effective in lowering BP, and are often needed to achieve a target value of BP in diabetic patients, especially in combination treatment (Aksnes, Skarn & Kjeldson, 2018).

Beta adrenergic blockers, also known as beta-blockers, are another antihypertensive drug class that can be effective in hypertensive patients with diabetes. Their use is not first line due to the risk of masking hypoglycemic symptoms and possibly exacerbating peripheral artery disease (Bakris, 2017). Therefore, these medications are to be avoided in patients with diabetes, especially those whom require insulin control as it can mask the symptoms of hypoglycemia leading to a diabetic coma. The use of medications within this drug class are prescribed when blood pressure is uncontrolled and are often used in combination with other agents. They have increased adverse effects with such as glucose intolerance resulting in slightly higher glycated hemoglobin concentrations (Marks, 1999). However, the benefits of these medications greatly outweigh the adverse effects, especially in management of cardiovascular disease. Beta blockers interfere with lipid metabolism and are associated with alteration of serum triglyceride and HDL-cholesterol concentrations (Podrid, 2016), resulting in decreased development of arteriosclerosis within the diabetic population.

The use of combined antihypertensive therapy is often preferred in part because blood pressure is multifaceted and requires multiple interventions to control. The use of diuretics combined with beta-blockers has been shown to reduce diabetic nephropathy. The combination of ACE inhibitors with diuretics and calcium channel blockers can reduce blood pressure and urinary albumin levels compared to any medication alone (Arauz-Pacheco, Parrott, and Raskin, 2002). There is no one medication used alone that will provide blood pressure stability within the

evidence-based parameters to minimize micro and macro vascular risks. However, if hypertension persists with monotherapy, then dual or combined therapy is recommended and even required in many patients with diabetes to control blood pressure.

Below is a helpful algorithm created by the American Diabetes Association Standards of Medical Care in Diabetes-2017 that can aid the clinician in choosing appropriate pharmacological interventions in people with diabetes.



### **Learning Points**

- The prevalence of hypertension and diabetes remains a growing problem in America and without early identification and treatment will result in the development of micro and macro vascular disease.
- Per the American Diabetes Association 2017 Guidelines and Joint National Committee Guideline 8, the goal blood pressure in patients with diabetes is a systolic less than 140 and a diastolic less than 90.
- In patients with additional comorbidities such as renal disease and cardiovascular disease, tighter blood pressure control is indicated. Therefore, the goal is for a systolic less than 130 and a diastolic less than 80.
- When initiating antihypertensive therapy, the use of an ACE inhibitor or an ARB is recommended as well as providing education on lifestyle modifications as control of blood pressure requires multiple interventions.
- People with multiple comorbidities require use of an intense antihypertensive such as beta-blockers and calcium channel blockers in combination with an ACEI or an ARB to prevent diabetic nephropathy.



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