

REVIEW ARTICLE

Hypertension and Diabetes: Risk, Interaction, and Management Target

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Abstract

Hypertension is generally defined as a sustained blood pressure higher than 140/90mmHg. Blood pressure should be brought closer to what's considered optimal: 120/80. An elevated blood pressure raises the risk for heart attack and stroke. Diabetes on the other hand, is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively utilize the insulin the pancreas produces, resulting in an impairment of the body's ability to process blood glucose. Insulin is a hormone that regulates blood sugar. On many occasions, the two occur together in the same patient. While the presence of hypertension in a patient tends to increase the risk of new-onset diabetes, presence of diabetes does also promote development of hypertension. In either scenario, the concomitant presence of the two medical conditions puts patients at a high risk of major cardiovascular complications. So the target of the physician in managing a patient with the duo conditions is to arrive at the recommended blood pressure levels to be achieved under pharmacological treatment in hypertension and diabetes. The paper reviews the risk of concomitant presence of the medical conditions, their pathophysiological mechanisms and the potential sites of therapeutic actions and interactions to achieve the target.

Keywords: Hypertension, diabetes mellitus, cardiovascular diseases, management target, renin-angiotensin system (RAS), insulin resistance.

Introduction

Hypertension

A medical condition in which a patient's blood pressure is consistently high over time is described as hypertension or high blood pressure. This condition poses a high risk for cardiovascular diseases such as coronary artery disease, stroke, heart failure, and peripheral arterial disease, when complicated, it could lead to vision loss and chronic kidney disease [1-3].

Classification of Hypertension

Primary hypertension is caused by non-specific lifestyle such as excess salt in the diet, over-weight, smoking and alcoholism habits [4]. This means the cause could not be tied to one specific factor; it could result from one or multiple factors, including: blood plasma volume, hormone activity in people who manage blood volume and pressure using medication. Environmental factors, such as stress and lack of exercise could also contribute.

Secondary hypertension may be caused by identifiable underlying ailments such as chronic kidney disease and/or narrowing of the kidney arteries. Use of birth control pills resulting in some endocrine disorders may also result in secondary hypertension [4].

Over 85% of cases seen by physicians are Primary hypertension, while about 15% live with Secondary hypertension [5]. Lifestyle changes and medications have been identified a ways of managing the condition, and indeed decrease the risk of health complications associated with it. These may include physical exercise to lose weight, abstinence from excessive salt intake, alcoholism and smoking. Where lifestyle changes are not sufficient, medications to lower the blood pressure are added [4].

Diabetes

This is a chronic disease associated with deficiency in the production of insulin by the pancreas. It could also result from the body's poor utilization of insulin produced by the pancreas. It is a condition that impairs the body's ability to process blood glucose. Insulin is a hormone that regulates blood sugar level [6]. Hyperglycaemia, a condition where blood sugar is elevated, is a condition associated with uncontrolled diabetes. When not properly managed, it could lead to serious damage to many of the body's systems such as nervous and vascular systems [6].

Type-1 Diabetes

Type-1 diabetes, also described insulin-dependent or childhood-onset diabetes, is characterized by low and insufficient insulin production, and requires daily administration of insulin. Type-1 diabetes is not preventable because its cause is largely unknown. It could present polyuria, polydipsia, constant hunger, excessive weight loss, vision impairment, and fatigue as symptoms. These symptoms may occur over time, and could also be sudden [7].

Type-2 Diabetes

Type-2 diabetes, also described as non-insulin-dependent diabetes, results from the body's ineffective use of insulin produced by the pancreas. This type, which largely results from physical inactivity and excess body weight constitute the majority of diabetic cases around the world. Clinical symptoms may be similar to those of type-1 diabetes, but are less noticeable at the onset. So, the disease may be diagnosed late, after complications may have set in [7].

Gestational Diabetes

Gestational diabetes results from excessive sugar in the blood during pregnancy. Though the blood glucose value may be lower than that of diagnostic diabetes, it's usually above normal. Women with this condition are at an increased risk of complications during gestation period and at parturition. In later life, the woman or the child or both become vulnerable to type-2 diabetes. Diagnosis of gestational diabetes is by through prenatal rather than presented symptoms [7].

Transition from Normality to Diabetes

In patients transiting from normality to diabetes, conditions such as impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) are common [8].

Risk

Diabetes and hypertension are frequently seen co-existing in a patient such that calls for concern. Hypertension in a patient suffering from diabetic tends to heighten the risk of cardiovascular diseases and associated complications [9].

Concomitant existence of of diabetes and hypertension in a patient makes cardiovascular prognosis difficult and affects the ability of achieving the recommended therapeutic targets, in terms of blood pressure levels and fasting glucose. This negative association between hypertension and diabetes of presents and promotes organ damage at cardiac, renal and vascular levels associated with hypertension. This may lead to a further increased risk of developing major cardiovascular events. Indeed, when hypertension coexists with diabetes, the risk of cardiovascular diseases (CVD) is heightened by about 75% [9,10].

Hypertension in type-2 diabetic patients clusters with other CVD risk factors such as microalbuminuria, central obesity, insulin resistance, dyslipidaemia, hypercoagulation, increased inflammation and left ventricular hypertrophy. The clustering risk factor in diabetic patients ultimately results in the development of CVD, which is the major cause of premature mortality in patients with type-2 diabetes [10]. This detrimental association between diabetes and hypertension has also been implicated in increased tissue inflammation, reactive oxygen species and insulin resistance, resulting in endothelial dysfunction, increased tissue renin-angiotensin-aldosterone system (RAAS) and increased sympathetic nervous system (SNS) activity [11].

Available data on this co-existence of the two show that common genetic and environmental factor promotes the two medical conditions [12]. Between 25 and 47% of hypertensive patients have insulin resistance or impaired glucose tolerance. With this glucose intolerance and insulin resistance, there are abnormal physiological tissue responses to insulin [12].

Interaction

Insulin resistance, diabetes and hypertension have somewhat complex and interwoven relationship. Patients with essential hypertension that are not treated have elevated fasting and postprandial insulin levels when compared with age- and sex-matched normotensive persons, regardless of body mass, indicating that there exists a direct correlation between plasma insulin levels and blood pressure (BP). But interestingly, the relationship between hyperinsulinaemia and hypertension is not seen in secondary hypertension, meaning that insulin resistance and hyperinsulinaemia are not consequences of hypertension, but rather a genetic predisposition that provides avenue for the two medical conditions [13].

Also, offspring of hypertensive parents show glucose metabolism impairment, indicating strong association between hypertension, diabetes and insulin resistance. In addition, correlation exists between up-regulation of RAAS, hypertension and diabetes, having effect on enhanced generation of ROS and could make an explanation for impaired glucose utilisation and hypertension associated with insulin resistance and type-2 diabetes. It has been proposed that increased autocrine/paracrine activity of angiotensin II results in diminished action of insulin and insulin growth factor-1 (IGF-1) communicating through the PI3K/Akt pathway, resulting in inhibition of mechanisms involved in the vasodilator and glucose transport properties of insulin and IGF-1 [5, 14].

Insulin initiates translocation of the GLUT4 glucose receptor to cell membrane by activating the PI3K/Akt system in skeletal muscle, adipose, and myocardial tissues. The unregulated angiotensin II acts through its receptor (AT1R) and results in formation of ROS and activation of low-molecular-weight G-proteins such as Rho A. Activation of these low-weight G proteins and the resultant promotion of the generation of ROS limits insulin/IGF-1 actions mediated through PI3K/Akt signaling, including activation of endothelial nitric oxide (NO) synthase (eNOS) activity, Na⁺ pump activation, and Ca²⁺-myosin light chain (MLC) de-sensitisation [15]. Similar RAAS-mediated increase in oxidative stress may contribute to insulin resistance in skeletal muscles. This is because ROS has been found to increase in skeletal muscle from Ren-2 rats that over-express tissue angiotensin II, and that this effect is abolished when the animals are treated with an AT1R blocker. This shows that therapy with angiotensin-converting enzyme inhibitors (ACE-I) will decrease the progression to type 2 diabetes in high-risk patients implying the critical role played by RAAS and useful role of ACE-I in the treatment of diabetes and hypertension [16].

Salt retention, volume expansion and resultant hypertension could also be a consequence of activation of the RAAS due to increased aldosterone secretion from the adrenal gland. Furthermore, aldosterone also contributes to hypertension decreasing parasympathetic activity and reducing baroreceptor sensitivity. Aldosterone may also lead to glomerulosclerosis and hypertension by increasing extracellular matrix deposition by glomerular cells [17]. Aldosterone receptor blockade in a Randomized Aldactone Evaluation Study (RALES) using spironolactone in moderate to severe heart failure patients may reduce by 30% [18]. Similarly, eplerenone, an antagonist of selective aldosterone receptor in patients with heart failure could equally decrease mortality rate [19]. Vasoconstrictive and volume-expanding actions of the RAAS may be enhanced by post-transcriptional mechanism to up-regulate vascular AT1Rs [20, 21].

Management Target

Management target should be a potent pharmacological intervention to reduce cardiovascular morbidity and mortality, particularly in the presence of diabetes mellitus is blood pressure reduction.

Lowering high blood pressure has been documented as beneficial, even in elderly patients with isolated systolic hypertension [22-25], essential hypertension [26-28], known cardiovascular risk profile, coronary artery disease, previous incident of stroke [29,30], and especially diabetes mellitus [31-40]. These have been used to support evidence for optimal blood pressure targets achievable and effective therapeutic strategies adoptable in patients with hypertension and diabetes. In patients with diabetes, a target BP of lower than 130/80mmHg is recommended in order to prevent death and disability associated with high blood pressure. Once hypertension is detected, both pharmacological (such as drugs) and non-pharmacological such as weight management and exercise) interventions are deployed. Instituting lifestyle modifications is equally helpful, along with medical therapy at the earliest detection of the pre-hypertensive patient.

The objective in hypertensive-diabetic would therefore be to initiate lifestyle changes, such as an improved diet, regular mild exercise, weight loss and abstinence from alcohol and smoking. Weight loss is so effective that it could take the place of medication [41].

Conclusion

Diabetes and hypertension could co-exist in a patient, with the presence of one increasing the risk of the other, suggesting a likely common genetic or pathophysiological process. The two medical conditions are associated with high risk of cardiovascular and renal diseases. This risk is even increased when the two conditions are present in a patient. Hypertension has to be controlled rigorously to decrease or prevent cardiovascular diseases and renal impairment. Insulin resistance, RAAS, endothelial dysfunction, and autonomic nervous system dysfunction constitute a vital part of the pathogenesis of the two conditions. Therapy aim should be to improve insulin sensitivity and RAAS blockade, as these may offer benefits where the two conditions exist concomitantly. Despite the impressive improvement in the clinical management of hypertension and diabetes, the achievement of effective control of therapeutic targets in these high risk patients remains a major clinical challenge. More prudent targets are the goal, especially when the two conditions are associated with other relevant co-morbidities.

References

1. Seriki AS (2017) Salt, Glucose, and Hypertension: Interactions Benefits and Risk. *J Cardiol Cardiovasc Ther* 4: 555634.
2. Lackland DT, Weber MA (2015) Global burden of cardiovascular disease and stroke: hypertension at the core. *Can J Cardiol* 31: 569-71.
3. Mendis S, Puska P, Norrving B (2011) Global atlas on cardiovascular disease prevention and control (PDF) (1st Edn.). Geneva: World Health Organization in collaboration with the World Heart Federation and the World Stroke Organization p. 38.
4. Poulter NR, Prabhakaran D, Caulfield M (2015) Hypertension. *Lancet* 386: 801-12.
5. Blendea M C, Jacobs D, Stump C S, McFarlane S I, Ogrin C, et al. (2005) Abrogation of oxidative stress improves insulin sensitivity in the Ren-2 rat model of tissue angiotensin II overexpression. *Am J Physiol Endocrinol Metab* 288: E353-9.
6. Wild S, Roglic G, Green A, Sicree R, King H (2004) Global Prevalence of Diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care* 27: 1047-53.
7. Pinhas-Hamiel O, Zeitler P (2005) The global spread of type 2 diabetes mellitus in children and adolescents. *J Pediatr* 146: 693-700.
8. Sowers J R, Epstein M, Frohlich E D (2001) Diabetes, hypertension, and cardiovascular disease: an update. *Hypertension* 37: 1053-59.
9. Sowers J R, Epstein M (1995) Diabetes mellitus and associated hypertension, vascular disease, and nephropathy. An update. *Hypertension* 26: 869-79.
10. Adler A I, Stratton I M, Neil H A W, Yudkin J S, Matthews D R, et al. (2000) Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. *BMJ* 321: 412-9.

11. Chabrot P, Cassagnes L, Alfidja A, Mballa JC, Nasser S, et al. (2010) Revascularization Of Traumatic Renal Artery Dissection By Endoluminal Stenting: Three Cases. *Acta Radiologica* 51: 21-6.
12. Sowers J R, Haffner S (2002) Treatment of cardiovascular and renal risk factors in the diabetic hypertensive. *Hypertension* 40: 781-8.
13. El-Atat F, McFarlane SI, Sowers JR (2004) Diabetes, hypertension, and cardiovascular derangements: pathophysiology and management. *Curr Hypertens Rep* 6: 215-23.
14. Sloniger JA, Saengsirisuwan V, Diehl CJ, Dokken BB, Lailerd N, et al. (2005) Defective insulin signaling in skeletal muscle of the hypertensive TG(mREN2)27 rat. *Am J Physiol Endocrinol Metab* 288: E1074-81.
15. Sowers JR (2004) Insulin resistance and hypertension. *Am J Physiol Heart Circ Physiol* 286: H1597-602.
16. Sowers J R (1999) Hypertension in Type II Diabetes: Update on Therapy. *J Clin Hypertens* 1: 41-7.
17. McFarlane S I, Sowers J R (2003) Cardiovascular endocrinology I: aldosterone function in diabetes mellitus: effects on cardiovascular and renal disease. *J Clin Endocrinol Metab* 88: 516-23.
18. Pitt B, Zannad F, Remme W J, Cody R, Castaigne A, et al. (1999) The Effect of Spironolactone on Morbidity and Mortality in Patients with Severe Heart Failure. *N Engl J Med* 341: 709-17.
19. Pitt B, Remme W, Zannad F, Neaton J, Martinez F, et al. (2003) Eplerenone, a Selective Aldosterone Blocker, in Patients with Left Ventricular Dysfunction after Myocardial Infarction. *N Engl J Med* 348: 1309-21.
20. Dengel D R, Hagberg J M, Pratley R E, Rogus E M, Goldberg A P (1998) Improvements in blood pressure, glucose metabolism, and lipoprotein lipids after aerobic exercise plus weight loss in obese, hypertensive middle-aged men. *Metabolism* 47: 1075-82.
21. Wassertheil-Smoller S, Blafox M D, Oberman A S, Langford H G, Davis B R, et al. (1992) The Trial of Antihypertensive Interventions and Management (TAIM) study. Adequate weight loss, alone and combined with drug therapy in the treatment of mild hypertension. *Arch Intern Med* 152: 131-6.
22. Staessen JA, Fagard R, Thijs L (1997) Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. *Lancet* 350: 757-64.
23. Liu L, Wang JG, Gong L (1998) Comparison of active treatment and placebo in older Chinese patients with isolated systolic hypertension. Systolic Hypertension in China (Syst-China) Collaborative Group. *J Hypertens* 16: 1823-9.
24. SHEP Cooperative Research Group (1991) Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). *JAMA* 265: 3255-64.
25. Beckett NS, Peters R, Fletcher AE (2008) Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 358: 1887-98.
26. Dahlof B, Devereux RB, Kjeldsen SE (2002) Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 359: 995-1003.
27. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (2002) Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 288: 2981-97.
28. Dahlöf B, Sever PS, Poulter NR (2005) Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet* 366: 895-906.
29. PROGRESS Collaborative Group (2001) Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet* 358: 1033-41.
30. Yusuf S, Diener HC, Sacco RL, Cotton D, Ounpuu S, et al. (2008) Telmisartan to prevent recurrent stroke and cardiovascular events. *N Engl J Med* 359: 1225-37.
31. Julius S, Kjeldsen SE, Weber M (2004) Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial. *Lancet* 363: 2022-31.
32. ONTARGET Investigators, Yusuf S, Teo KK (2008). Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med* 358: 1547-59.
33. Yusuf S, Teo K, C Anderson, J Pogue, L Dyal, et al. (2008) Effects of the angiotensin-receptor blocker telmisartan on cardiovascular events in high-risk patients intolerant to angiotensin-converting enzyme inhibitors: a randomised controlled trial. *Lancet* 372: 1174-83.
34. Pepine CJ, Handberg EM, Cooper-DeHoff RM (2003) A calcium antagonist vs a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease. The International Verapamil-Trandolapril Study (INVEST): a randomized controlled trial. *JAMA* 290: 2805-16.
35. Fox KM (2003) EUROpean trial on reduction of cardiac events with Perindopril in stable coronary Artery disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). *Lancet* 362: 782-8.
36. Bosch J, Yusuf S, Hertz C Gerstein, Pogue J, Sheridan P, et al. (2006) Effect of ramipril on the incidence of diabetes. *N Engl J Med* 355: 1551-62.
37. NAVIGATOR Study Group, McMurray JJ, Holman RR (2010) Effect of valsartan on the incidence of diabetes and cardiovascular events. *N Engl J Med* 362: 1477-90.
38. Wassertheil-Smoller S, Blafox M D, Oberman A S, Langford H G, Davis B R, et al. (1992) The Trial of Antihypertensive Interventions and Management (TAIM) study. Adequate weight loss, alone and combined with drug therapy in the treatment of mild hypertension. *Arch Intern Med* 152: 131-6.
39. Sacks F M, Svetkey L P, Vollmer W M, Appel L J, Bray G A, et al. (2001) Effects on Blood Pressure of Reduced Dietary Sodium and the Dietary Approaches to Stop Hypertension (DASH) Diet. *N Engl J Med* 344: 3-10.
40. Halbert J A, Silagy C A, Finucane P, Withers R T, Hamdorf P A (1999) Exercise training and blood lipids in hyperlipidemic and normolipidemic adults: a meta-analysis of randomized, controlled trials. *Eur J Clin Nutr* 53: 514-22.
41. Whelton S P, Chin A, Xin X, He J (2002) Effect of Aerobic Exercise on Blood Pressure: A Meta-Analysis of Randomized, Controlled Trials. *Ann Intern Med* 136: 493-503.