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Treatment of Hypertension in Patient with Diabetes

Mayurgiri R. Gauswami[1], Shweta V. Sankhat[1], Jinal R. Kantariya[1], Ruhin M. Khokhar [1], Sakshi M. Rathod[1], Vruti M. Lumbhani [1]

[1] Gyanmanjari Pharmacy College, Bhavnagar 364001, Gujrat, India.

ABSTRACT

Hypertension, or high blood pressure, is common in people with diabetes (20-60%). It's a significant risk factor for heart issues and complications like eye and kidney problems. Cardiovascular disease is the main cause of death in those with diabetes (86%). Until recently, not much research focused on diabetes and hypertension. Recent studies show treating high blood pressure in diabetes patients effectively reduces complications. Aggressive diagnosis and treatment are recommended to reduce the risk of heart and other complications.

Epidemiological studies and trials define high blood pressure differently in diabetic patients. In the general population, even a small increase in blood pressure raises cardiovascular disease risk. For diabetics, higher diastolic pressure (above 70 mmHg) is linked to more severe eye issues. Past definitions of high blood pressure (160/90 mmHg) for diabetics are considered too high now. In 1997, new guidelines suggested lower targets (130/85 mmHg) for diabetic patients compared to the general population. Recent evidence shows benefits in outcomes by keeping blood pressure below 140/80 mmHg for diabetics, and even lower for elderly populations with systolic hypertension. So, the goal for blood pressure in diabetic patients is 130/80 mmHg.

Hypertension (high blood pressure) is 1.5–3 times more common in people with diabetes compared to those without diabetes of the same age. In type 1 diabetes, it usually develops after several years, mainly due to diabetic kidney issues, affecting about 30% of individuals. For type 2 diabetes, hypertension may be present at diagnosis or even before high blood sugar develops. Factors like age and obesity in type 2 diabetes make it challenging to pinpoint the exact influence of diabetes on hypertension. After adjusting for age and weight, hypertension is still 1.5 times more prevalent in people with diabetes. About 20–60% of type 2 diabetes patients may develop hypertension, influenced by age, ethnicity, and obesity. In certain ethnic groups, kidney issues may be a major cause. The combination of hypertension, high blood sugar, high cholesterol, central obesity, and insulin resistance is common in diabetes, leading to increased risks of heart disease, kidney problems, and eye issues. The link between diabetic nerve damage and high blood pressure is less clear but might be a contributing factor.

Pathophysiology

When kidney issues (nephropathy) are present in diabetes, there's an increase in body fluid and sodium. The system regulating fluids (RAAS) is less active, causing volume-dependent hypertension. Without diabetic nephropathy, other factors contribute to hypertension—both genetic and acquired. Some people with hypertension have higher insulin levels due to insulin resistance and reduced insulin clearance. This hyperinsulinemia might lead to increased sodium absorption by the kidneys and overactivity in the nervous system, causing hypertension, especially in obese individuals and those with insulin resistance like in type 2 diabetes. Insulin resistance is also linked to poor blood vessel response to insulin in muscles and increased response to constricting substances. However, the complete role of insulin resistance in causing hypertension is not entirely clear.

Screening and evaluation

All diabetes patients should have their blood pressure checked at diagnosis and during regular visits, aiming to keep it below 130/80 mmHg due to high cardiovascular risk. The assessment includes a detailed medical history, focusing on heart risk and diabetes-related issues. Blood pressure should be measured while sitting and standing, with multiple readings for accuracy, especially in diabetic patients with nervous system issues. Diagnosis of hypertension in diabetes requires consistent readings over 130/80 mmHg on two separate occasions. Physical exams should check height, weight, eyes, and arteries. Initial tests include kidney function, electrolytes, A1C for glucose control, cholesterol levels, and urinary albumin to assess kidney health.

Behaviour treatment

Managing diet with moderate sodium restriction effectively lowers blood pressure in people with essential hypertension. Weight loss is also beneficial, independently reducing blood pressure and improving glucose and lipid levels. Losing 1 kg of body weight can lower blood pressure by around 1 mmHg.

While very low-calorie diets and weight-loss drugs haven't been thoroughly studied for diabetic hypertension, caution is advised with certain appetite suppressants, as they may increase blood pressure. Weight reduction is considered effective for mild-to-moderate hypertension in initial management.

Sodium restriction hasn't been specifically tested in diabetic populations but has shown a 5 mmHg reduction in systolic and 2–3 mmHg in diastolic blood pressure in essential hypertension. Even with medications, combining them with salt restriction often enhances effectiveness. The impact of these measures on diabetic individuals is uncertain.

Moderate physical activity, like brisk walking, helps lower blood pressure. Quitting smoking and moderating alcohol intake are recommended. Studies suggest a link between calcium, magnesium, and potassium intake and blood pressure, but data specific to diabetic hypertension is lacking. Trials on calcium supplementation show a small blood pressure reduction, while there's a lack of randomized trials on magnesium in diabetic individuals with hypertension.

Drug therapy

The goal of antihypertensive treatment is to lower blood pressure and prevent complications like heart failure, heart disease, stroke, and issues with small blood vessels in organs. Different medications have similar effects on blood pressure, but small differences in their effectiveness have been observed. However, how these differences impact actual health outcomes is not well understood. Studies have also looked at how these medications affect other health markers like cholesterol and blood sugar, which are risk factors for heart issues, but their impact on real-life outcomes is not entirely clear.

Effects of antihypertensive drugs on microvascular complications Nephropathy

Antihypertensive drugs aim to prevent complications like kidney problems in diabetes. About 20-30% of type 1 and 10-20% of type 2 diabetes patients may develop severe kidney issues. Diabetes is a major cause of end-stage renal disease (ESRD), especially in certain ethnic groups. Clinical interventions aim to reduce the impact of this complication on health. Studies have examined the effects of these drugs on markers of kidney damage, such as albumin in urine. While some studies focus on clinical outcomes, others emphasize renal function measures. Managing high blood pressure has shown evidence in preventing advanced kidney disease and related mortality. Notably, patients with normal blood pressure and diabetic kidney issues progress more slowly than those with high blood pressure. Studies have explored the impact of antihypertensive treatments, including ACE inhibitors, on slowing down kidney problems, even in patients without high blood pressure

Type 1 patient

In a study with type 1 diabetic patients, using the ACE inhibitor captopril led to a significant decrease in kidney issues. This trial compared captopril to other antihypertensive drugs. Patients taking captopril had a slower decline in kidney function compared to those on a placebo. The study found a 50% reduction in endpoints like death, severe kidney disease, or doubling of serum creatinine with captopril compared to standard antihypertensive treatment. Interestingly, the small differences in blood pressure between the groups suggested that ACE inhibitors like captopril might protect the kidneys independently of their blood pressure-lowering effects. Similar benefits were observed in studies involving patients with microalbuminuria (early sign of kidney trouble) and hypertension. Even in type 1 diabetic patients with microalbuminuria but without hypertension, ACE inhibitors were found to be helpful in delaying or preventing the progression of kidney problems.

Type 2 Patient

In a study with type 2 diabetic patients, the UK Prospective Diabetes Study (UKPDS) looked at different blood pressure control levels and their effects on complications. Tight control (goal: blood pressure <150/85 mmHg) showed a 24% reduction in diabetes-related issues, 32% in diabetes-related deaths, and 37% in microvascular problems (kidney and advanced eye issues). For kidney health, tight control reduced the risk of developing high urinary albumin levels by 29% at 6 years. However, it didn't significantly impact overt proteinuria or increased plasma creatinine levels.

There's limited evidence that ACE inhibitors prevent diabetic nephropathy in type 1 or type 2 patients without microalbuminuria. Angiotensin receptor blockers (ARBs), like losartan and irbesartan, have shown promise in slowing albuminuria progression and nephropathy development in hypertensive type 2 diabetic patients. Large trials suggest ARBs have renal protective effects beyond blood pressure reduction.

Effects of antihypertensive drugs on cardiovascular disease in diabetic patient*

Various studies suggest that controlling blood pressure effectively in diabetic patients can reduce cardiovascular events. In the UK Prospective Diabetes Study (UKPDS-HDS), tight blood pressure control showed a 24% drop in total diabetes-related issues, a 32% decrease in diabetes-related deaths, and a 44% decrease in strokes.

Comparing dihydropyridine calcium channel blockers (DCCBs) and ACE inhibitors, the ABCD trial indicated a higher risk of myocardial infarction with DCCBs. The FACET study reported fewer cardiovascular events with the ACE inhibitor fosinopril compared to the DCCB amlodipine.

In a broader analysis, studies involving patients with diabetes and hypertension showed favorable outcomes with antihypertensive treatment, reducing overall mortality and cardiovascular events. For instance, the Systolic Hypertension in Europe trial found a significant reduction in cardiovascular events in diabetic patients receiving antihypertensive treatment compared to those on placebo.

In the Systolic Hypertension in the Elderly (SHEP) study, diabetic patients aged over 60 receiving the diuretic chlorthalidone experienced a 34% reduction in cardiovascular events compared to a placebo group. The Hypertension Optimal Treatment (HOT) trial involving 1,501 diabetic patients found that targeting a diastolic blood pressure below 80 mmHg resulted in a marked reduction in major cardiovascular events and cardiovascular mortality.

Studies comparing different drug classes on cardiovascular outcomes showed varying results. The Swedish Trial observed fewer myocardial infarctions with ACE inhibitors compared to certain calcium channel blockers. The International Nifedipine study found no difference between nifedipine and a diuretic combination. The Nordic Diltiazem Trial suggested lower stroke risk with diltiazem but a potential increase in other cardiovascular issues.

In the Captopril Prevention Project (CAPPP), diabetic patients taking captopril had a 14% lower rate of combined cardiovascular outcomes compared to those on diuretics and beta-blockers. The HOPE study, involving patients at high cardiovascular risk, found that the ACE inhibitor ramipril significantly decreased all-cause and cardiovascular mortality, as well as cardiovascular events like heart attacks and strokes.

Agent

Thiazide diuretics are medications that reduce sodium and have shown effectiveness in lowering stroke and heart failure risks in hypertension. They can cause side effects like low potassium and sodium levels. In elderly individuals with isolated systolic hypertension, thiazides have reduced cardiovascular issues. However, retrospective studies suggested increased cardiovascular mortality in diabetic patients taking diuretics, but these studies had limitations.

Loop diuretics, another type, decrease sodium significantly and are recommended for patients with decreased renal function. They may lead to low potassium and sodium levels.

Adrenergic blockers, like centrally acting agents and beta-blockers, lower blood pressure but may have side effects such as drowsiness and impotence. Centrally acting agents decrease central sympathetic outflow, and beta-blockers can affect B1- and B2-receptors. Atenolol, a selective beta-blocker, has shown effectiveness in reducing proteinuria and complications in diabetic hypertensive patients.

Concerns have been raised about the impact of beta-blockers on hypoglycemia perception and recovery, but evidence is inconclusive. In patients with a history of severe hypoglycemia using insulin, caution is advised, but in other cases, especially after a heart attack, the benefits of beta-blockers likely outweigh potential risks.

Calcium channel blockers (CCBs) inhibit calcium influx, causing vasodilation. There are three subclasses: dihydropyridines (DCCBs), benzothiazepines, and phenylalkylamines. DCCBs mainly dilate blood vessels and may be effective as antihypertensive agents. However, there's conflicting evidence on their cardiovascular benefits, and combining them with other drugs makes it challenging to assess their standalone effectiveness.

A recent analysis suggests that CCBs may be similar to other drugs in protecting against stroke but less effective against heart attacks. Interpretation of clinical trials using DCCBs is complex due to differences between drugs.

In diabetic nephropathy, some studies show increased proteinuria with nifedipine, but long-term effects are unclear. DCCBs generally have a neutral impact on metabolic parameters.

ACE inhibitors are beneficial in managing hypertension in diabetic patients, preventing cardiovascular complications, and retinopathy progression. The recent HOPE trial indicates potential benefits beyond blood pressure control, possibly due to effects on the endothelium and various substances.

In summary, the choice of antihypertensive medication for diabetic patients involves considering individual factors and potential benefits, such as cardiovascular and renal protection.

BP in patients

For diabetic patients, maintaining optimal blood pressure is crucial. Studies like UKPDS and HOT show better outcomes with tighter control (e.g., diastolic blood pressure around 80 mmHg). The ABCD trial indicates benefits, with decreased mortality when aiming for 75 mmHg diastolic pressure. Generally, targeting around 130/80 mmHg is reasonable, supported by epidemiological evidence. While going lower might further reduce risk, it increases costs and potential side effects, making it challenging in practice. Remember, there's no fixed threshold, and risk decreases even within the normal range.

Conclusion

In summary, all diabetes patients should regularly check their blood pressure. Those with readings above 130/80 mmHg may need treatment. Initial approaches involve lifestyle changes, like reducing sodium and alcohol, and increasing physical activity. If blood pressure remains high, medications like ACE inhibitors, ARBs, thiazide diuretics, or β-blockers are recommended. Adjustments or additional drugs may be needed to achieve the target of around 130/80 mmHg. Thiazide diuretics are effective in improving outcomes. Classes like NDCCBs can be used when others aren't tolerated. Treatment should

be personalized based on patient characteristics and preferences. Regular monitoring is crucial, and aggressive control is beneficial for cardiovascular health. Individualized decisions should consider factors like comorbidities, tolerability, and cost.

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