This weeks Question:

Which is better to treat hypertension in patients with diabetes?

1. **Ace Inhibitors**
2. **Calcium Channel Blockers**
3. **Thiazide Diuretic + Beta Blocker**
4. **An ARB**
5. **Any of the Above**

The correct answer is 5, any of the above. There is no one product that works for everyone, In hypertensive diabetic patients, lower the blood pressure to target by any means, but choose a combination that best suits the individual patient.

This is a 2-part question that addresses the treatment of hypertension and the prevention of renal disease. Numerous recent studies have shown that lowering blood pressure reduces cardiovascular morbidity and mortality in human diabetes.[1] There does not appear to be any lower limit of blood pressure at which benefit is not seen. The Hypertension Optimal Treatment (HOT) study[2] showed continuing benefit with diastolic pressures lowered to 80 mm Hg. The importance of systolic hypertension has become more apparent lately and recommended blood pressure targets of 130/85 mm Hg or 140/80 mm Hg have been proposed by the World Health Organization (WHO)[1] and British Hypertension Society,[3] respectively.

To date, there appears to be no benefit of one class of agent over another. Older drugs, such as thiazides and beta-blockers, are as effective as newer agents.[1] Low-dose thiazides (eg, bendroflumethiazide 2.5mg, hydrochlorothiazide and chlorthalidone 12.5mg) seem metabolically safe in diabetes. Beta-blockers may promote glucose intolerance however and seem less well tolerated than ACE inhibitors, at least in 1 study.[4] However, they are probably more effective postmyocardial infarction in diabetic than in nondiabetic subjects. The concern about dihydropyridine calcium channel blockers following results from Appropriate Blood Pressure Control in Diabetes (ABCD)[5] study and Fosinopril versus Amlodipine Cardiovascular Events Trial (FACET)[6] does not seem justified since the publication of results from Systolic Hypertension in Europe (SystEur)[7] and HOT. Doxazosin monotherapy should be used with caution however following the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack (ALLHAT) study decision to withdraw it.[8]

Results from the recently published Heart Outcomes Prevention Evaluation (HOPE) and MICRO-HOPE Study[9] suggest a benefit of ramipril in reducing cardiovascular morbidity and mortality in high-risk type-2 diabetic patients, two thirds of whom were said to be hypertensive. However, no data on concomitant therapies are given and the added risk of hypertension alone may not be that strong.

Thus, the important message is that in hypertensive diabetic patients, lower the blood pressure to target by any means, but choose a combination that best suits the individual patient.

The prevention of renal disease is more difficult to answer in some ways but easier in others. The difficult part is that few studies have used hard end points, such as renal failure or **reduction in** glomerular filtration rate. Most have reported an effect on proteinuria or albuminuria and used this as a surrogate. It is still not clear whether reduced proteinuria equates to renal functional preservation in human diabetes. Moreover, in many studies, it has been difficult to dissociate benefits in terms of reduction of proteinuria as being due to particular agents or to concomitant reduction in blood pressure. The easy part of the answer is that, for the most part, ACE inhibitors show a greater propensity to lower albuminuria than other agents.

Primary prevention in the context of albuminuria would mean prevention into the microalbuminuric range (20-200mcg/min or 30-300mg/d). Some studies using ACE inhibitors in type-1 patients have demonstrated such an effect but data in type-2 patients are more scarce.[10]

Secondary prevention could be defined as a reduction in the numbers of patients progressing to clinical nephropathy (albuminuria > 300 mg/d) and many studies in microalbuminuric type 1 and 2 patients with and without hypertension have shown that ACE inhibitors are effective in this regard.[11,12] There are also data showing that beta-blockers and calcium channel blockers are also effective in this regard, but on balance the degree of reduction of albuminuria is less.[11,12]

Only 1 study has shown a benefit of ACE inhibitors on the development of end-stage renal disease, the Collaborative Study Group Trial in proteinuric type-1 patients.[13] This could be considered to be evidence of tertiary prevention. Two large studies in type-2 patients with nephropathy that are comparing angiotensin II receptor antagonists and calcium channel blockers are due to report next year.

In terms of preventing renal disease, most endo's probably use ACE inhibitors as first-line treatment in patients with type 1 or type 2 diabetes who have increased albuminuria regardless of their blood pressure; although in practice, many will be hypertensive by modern definitions.[1,3] Whether these drugs should be used in normoalbuminuric and normotensive subjects is a hotly debated topic. As a final point, it important to mention that increased albuminuria is often associated with other cardiovascular risk factors including hyperlipidemia and smoking. These will also need vigorous correction.

References

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