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Letters to the Editor

Enalapril retards glomerular basement membrane thickening and albuminuria in the diabetic rat: are these effects specific for enalapril?

Dear Sir,

Cooper et al. [1] recently reported that enalapril (35 mg/l in drinking water) retarded the development of glomerular basement membrane thickening and albuminuria in hypertensive and normotensive diabetic rats. The results obtained from this well-designed study are of interest in view of the recent debates on potential nephroprotective potencies of various antihypertensive agents in diabetic patients. However, we wonder whether the reported effects of enalapril [1] are due to some specific pharmacological action of angiotensin converting enzyme (ACE) inhibitors or merely due to the reduction of blood pressure which was observed both in hypertensive and normotensive rats.

The same group of investigators have already reported in September 1988 at the EASD satellite symposium "Hypertension Associated with Diabetes Mellitus" that enalapril (35 mg/l) and a combination of hydralazine (50 mg/l) and metoprolol (50 mg/l) were equivalent in hypotensive efficacy and in reduction of albuminuria in hypertensive diabetic rats [2]. Furthermore, at the 4th European Meeting on Hypertension in Milan, Italy, this year, the same authors reported that antihypertensive therapy with enalapril (35 mg/l) or a combination of hydralazine (50 mg/l) and metoprolol (50 mg/l) ameliorated functional (albuminuria) and structural (glomerular basement membrane thickness) parameters of nephropathy in the hypertensive diabetic rat and that there was no advantage of ACE-inhibition over the combination regimen [3]. In fact, the results of these comprehensive serial studies by Cooper et al. [1-3] suggest that the reported effects of enalapril [1] are not specific for this class of agents but rather due to the blood pressure reduction.

We are concerned about the possibility that the article [1] might give an impression that only enalapril or ACE-inhibitors possess such renal effects. It would have been more informative for our readers if they could have presented their interesting data [2, 3] in total [4] in the recent paper in Diabetologia.

Yours sincerely,
T. Baba and P. T. Sawicki

References

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2. Cooper ME, Allen TJ, Macmillan PA, Jerums G, Doyle AE (1988) Experimental diabetic nephropathy - the role of genetic hypertension and antihypertensive therapy. Abstract Book of Second International Symposium on Hypertension Associated with Diabetes Mellitus, Paris, September 8-10, p 19
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Response from the authors

Dear Sir,

In response to the letter by T. Baba and P. T. Sawicki, we agree completely with their suggestions that the effects of enalapril in retarding glomerular basement membrane thickening and albuminuria in normotensive and hypertensive diabetic rats that we recently reported [1], may be due to reduction of blood pressure rather than via a specific pharmacological action of angiotensin converting enzyme (ACE) inhibitors. The possibility that a major effect of ACE inhibition is via reduction in systemic blood pressure is discussed in the manuscript.

The manuscript was originally submitted to Diabetologia in November 1988. However, after editorial review, we were asked to alter the manuscript to a Rapid Communication format and therefore more detailed discussion of the specificity of the effects of the ACE inhibitors could not be included. However, as outlined in the last sentence of our published manuscript, we believe that the specificity of ACE inhibitors in diabetic renal disease remains an open question. Obviously, after obtaining the results of ACE inhibition therapy on diabetes related glomerular ultrastructural abnormalities, it was decided to repeat the experiment directly comparing ACE inhibition with conventional antihypertensive therapy. It is important to appreciate that glomerular ultrastructural assessment by quantitative histomorphometry is a time consuming procedure which significantly delays the ultimate analysis of experimental studies despite completion of the study protocol and measurement of albuminuria. These long-term experiments are at present being completed. Preliminary results on albuminuria [2] and glomerular ultrastructure [3] in pilot groups have now been reported in abstract form. As yet, analysis of all the data is not complete, nor have the data been submitted as a manuscript to any journal.

In this highly controversial area, we believe that until our present experiments comparing ACE inhibition with conventional antihypertensive therapy have been completed, it would be inappropriate for us to make definitive statements about the specificity of ACE inhibition in diabetic renal disease.

Yours sincerely,
M. Cooper, G. Jerums and A. E. Doyle

References

1. Cooper ME, Allen TJ, Macmillan PA, Clarke BE, Jerums G, Doyle AE (1989) Enalapril retards glomerular basement membrane thickening and albuminuria in the diabetic rat. Diabetologia 32: 326-328
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