Anti-proteinuric effect of losartan: statistical vs clinical significance

Sir,
We read with great interest the recent article on the anti-proteinuric effect of losartan when compared with amlodipine [1]. Though we agree with the findings of the authors, we are unable to assess the clinical significance of this article from the data provided. A perusal of table 1 (Baseline characteristics) indicates that the patients receiving losartan had considerably more proteinuria compared with the amlodipine group (3.1 g vs 2.5 g), therefore potentially the decrease in proteinuria with treatment could be greater in the losartan group as the baseline risks were higher. In spite of the randomization process, details on the randomization procedure (i.e. random allocation sequence), allocation concealment and the implementation of allocation sequence (as required by the CONSORT statement [2]) have not been provided in the current study.

The results of a decrease in proteinuria (32.4% at 4 weeks and 50.4% at 20 weeks), though impressive, have been averaged for the group and it is impossible to truly appreciate the clinical significance of this study. Numbers needed to treat (NNTs), which is the reciprocal of absolute risk reduction (ARR) are a better measure of clinical significance than relative risk reduction and statistical significance [3]. It would be meaningful to pre-determine a useful decrement of proteinuria and determine what proportion of patients treated with losartan when compared with amlodipine achieved this. A recent study, however, indicates that journals infrequently report NNTs despite recent wide practice of evidence-based health care [4]. The results of the current study, though statistically highly significant, would be more meaningful if the results were presented in such a way as to be able to calculate the NNT and ARR, thereby increasing the ability of the nephrologist to calculate the true clinical significance of the article. The long-term outcome of change of surrogate markers, i.e. a decrease in proteinuria and in urinary TGF-β, on overall morbidity due to renal insufficiency remains to be studied in long-term outcome-based studies.

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Reply

Sir,
A. K. Ghosh and K. Ghosh are concerned about some aspects of our study [1]: they point out that baseline proteinuria levels were higher in the losartan group: 3.1 g/24 h (2.5–3.8) compared with 2.5 g/24 h (2.3–3.2) in the amlodipine group and that this difference could influence the greater antiproteinuric response of patients treated with losartan. However, we would like to stress that this difference in baseline proteinuria between groups was not significant and that the antiproteinuric response was independent of the level of proteinuria at baseline, when considering the whole group of 97 randomized patients and patients of the losartan and amlodipine groups separately. With respect to the randomization process, it followed the usual requirements, as itemized in the CONSORT statement [2]. Taking into account the objectives and the primary and secondary end points of our study (decrease in the level of proteinuria and changes in the plasma and urinary levels of TGF-β), we think that the statistical approach proposed by A. K. Ghosh and K. Ghosh (NNT, number needed to treat) would not add useful information to the study. On the contrary, we think that the results of our study, showing a drastic proteinuria decrease (~50.4% at week 20) in our non-diabetic patients treated with losartan will be of great interest for any skilled nephrologist aware of the fundamental clinical importance that such antiproteinuric responses represent in terms of future renoprotection. Confirming preliminary studies [3], all the multicentre studies of the last years with angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs) or the combination of an ACEI plus ARB, in both diabetic and non-diabetic proteinuric diseases, have consistently demonstrated that the renoprotection induced by these drugs is predicted by and closely related to their antiproteinuric efficacy [4–9]. In fact, on the basis of this accumulated clinical experience [10], we and others believe that proteinuria decrease should be considered as a surrogate marker of renoprotection in proteinuric nephropathies.

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2. Moher D, Schultz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of