ACE gene I/D polymorphism and the presence of renal failure or hypertension in autosomal dominant polycystic kidney disease (ADPKD)

Sir,

Epidemiological data have suggested that interactions between multiple genetic and environmental factors are involved in the process of progressive renal damage in the course of various kidney diseases, including autosomal polycystic kidney disease [1–4].

Recently, we read with interest the results of a meta-analysis of studies examining the association between angiotensin I-converting enzyme (ACE) gene insertion/deletion (I/D) polymorphism and the presence of end-stage renal disease (ESRD) in patients with ADPKD [5]. Based on the analysis of combined data from 13 reports, Pereira et al. [5] found no proof for the involvement of ACE gene I/D marker in the development of ESRD or hypertension in ADPKD patients.

Inspired by this report, we looked into ACE I/D genotypes obtained in a small sample of 105 Caucasian ADPKD patients [58 women and 47 men, median age 43 years (25–75%: 35–54 years)], of whom 42 presented renal failure (S-creatinine ≥ 130 μmol/l), with median serum creatinine of 432 μmol/l (25–75%: 192–780 μmol/l). Seventy patients were hypertensive (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, or antihypertensive treatment). There were no significant differences in I/D genotype distributions between ADPKD patients, with and without renal failure. Frequencies of D/D, I/D and I/I genotypes among patients with renal failure were 33, 57, and 9%, respectively. Frequencies of D/D, I/D and I/I genotype frequencies were 34, 57 and 9%, while in normotensives, they were 34, 43 and 23%, respectively.

In summary, our data obtained in a small sample of ADPKD patients failed to show an association between the ACE gene polymorphism and the presence of renal failure or hypertension, and can be added to further meta-analyses of ADPKD patients.

Conflict of interest statement. None declared.

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in the diagnosis of infected cysts [4]; $^{111}$Indium-labelled leucocyte scans and fine needle aspiration and cytology may also be helpful. The final diagnosis was made by imaging in only 25 (41%) cases and by non-radiological tests in 15 (24.6%) cases, and so the place of non-imaging tests in the diagnosis of inter-current abdominal problems should not be overlooked. The measurement of inflammatory markers (i.e. C-reactive protein), white cell count, mid-stream urine (with blood cultures if pyrexial) is therefore recommended in all presentations with acute abdominal pain and/or haematuria.

Although clinical accuracy of diagnosis was generally good, absence of a consistent protocol for investigation resulted in frequent unnecessary investigations. We have, therefore, designed a simple algorithm incorporating clinical, laboratory and radiological assessment, that we are now implementing, for investigation of all such clinical presentations in ADPKD to avoid unnecessary diagnostic work up (Figure 1).

Conflict of interest statement. None declared.


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**Erythropoietin and its lost receptor**

Sir,

Several reports have recently appeared in the literature, suggesting that commercially available anti-erythropoietin receptor (EpoR) antibodies may not be suitable for the immuno-histochemical detection of EpoR. Elliott et al. [1] have pointed out that H 194, M-20 and C-20 antibodies cannot be used to detect EpoR expression, as they cross-react with non-EpoR proteins due to their low specificity and affinity [1,2]. We tested three rabbit polyclonal anti-peptide anti-EpoR antibodies already investigated by Elliott, C-20, M-20 and H-194 (by Santa Cruz Biotechnology). In addition, we used a mouse monoclonal antibody, MAB 307 (by R&D). The study was conducted on rat and human kidney, which expresses EpoR, and on human tubular tumoural cell cultures (769 P), which do not express EpoR, using western blotting (WB), immunofluorescence and immunostiochemistry. In WB, C-20 and H-194 recognized many non-specific bands with different molecular weights. M-20 detected a 59 kDa protein compatible with EpoR on renal tissue; in the 769 P cell line M-20 recognized only a 30 kDa band. MAB 307 identified a 59 kDa protein in renal tissue and no band in the cell line. Thus, only a comparative evaluation with WB using M-20 and/or MAB 307 antibodies could assess EpoR expression.

Immunoperoxidase staining conducted on formalin-fixed and paraffin-embedded rat and human renal tissue showed heterogeneous patterns. M-20 identified proximal tubular cells nucleus and cytoplasm, while the cell membranes showed a weaker staining (Figure 1). C-20 localized in distal tubular cells cytoplasm, while H-194 showed an intense staining in tubular brush border (Figure 2). MAB 307 did not show a specific staining. We expected a positive staining in endothelium of blood vessel and glomerular capillaries [3], but none of the tested antibodies marked glomerular endothelium and peri-tubular interstitial vessels.

In immunofluorescence C-20 antibody diffusely marked renal tissue. H-194 localized in the tubular cell bodies in the brush border and in glomerular endothelium. M-20 marked a limited number of tubules, both the cell membrane and the brush border, glomerular endothelium and podocytes. MAB 307 staining seems to be limited to a small portion of tubular basal membrane and involved the vessel wall.