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The effect of angiotensin type 1 receptor blockade on adhesion molecules in patients with IgA nephropathy

Sir,

Various studies have linked inflammation and endothelial dysfunction in patients with chronic renal disease [1]. Plasma levels of adhesion molecules [soluble intracellular adhesion molecule-1 (sICAM) and soluble vascular adhesion molecule-1 (sVCAM)] are markers of endothelial dysfunction and also risk factors for cardiovascular disease in patients with IgA nephropathy (IgAN) [2]. It is known that vascular lesion begins long before its clinical manifestation and its pathogenesis involves endothelial dysfunction and low-grade inflammation. Numerous studies provide evidence that ACE inhibitors or angiotensin II receptor antagonists (ARBs) are more effective than other antihypertensive drugs in slowing the progressive decline in glomerular filtration rate in IgAN [3]. Our aim was to test whether blocking the renin–angiotensin system (RAS) with irbesartan decreases levels of adhesion molecules in patients with biopsy-proven IgAN.

We included in our study 36 patients (M/F 26/10, 51 ± 12.5 years). The inclusion criteria were biopsy-proven IgAN (defined by standard morphologic and immunohistochemical criteria), serum creatinine $\leq$1.5 mg/dl and urinary protein excretion $\geq$500 mg/day in at least three consecutive determinations during the previous 6-month period. Exclusion criteria were diabetes mellitus, coronary artery disease, peripheral vascular disease, stroke, acute infection or the inflammatory process on course and marked hypercholesterolaemia. Blood samples were collected from all patients before (*T*0) and after 16 weeks (*T*1) of treatment with 300 mg of irbesartan given once daily in the morning. A thorough blood chemistry control was performed in all patients. Creatinine clearance was determined by using venous blood for serum levels of creatinine and a 24-h urine collection. Serum and urinary creatinine concentration was measured using the Jaffé method. Serum intercellular adhesion molecule-1 and vascular cell adhesion molecule-1 were measured by immunosorbent assay (ELISA). Statistical analyses were performed using SPSS version 13.0 (SPSS, Chicago, IL, USA).

Systolic (SBP) and diastolic blood pressure (DBP) was significantly lower after irbesartan was given (from SBP *T*0: 144 ± 19 mmHg DBP *T*0: 93 ± 9 mmHg to SBP *T*1: 129 ± 9 mmHg DBP *T*1: 88 ± 8 mmHg, $P < 0.01$). Proteinuria levels were also significantly lower after treatment: from 1.6 ± 0.7 g/24 h − *T*0 to 1.1 ± 0.9 g/24 h − *T*1 ($P < 0.001$). We observed a significant decrease of sICAM and sVCAM plasma levels in patients after treatment with irbesartan (sICAM *T*0: 628 ± 163 ng/ml to sICAM *T*1: 369 ± 112 ng/ml, $P < 0.001$; sVCAM *T*0: 1028 ± 649 ng/ml to sVCAM *T*1: 688 ± 248 ng/ml, $P < 0.001$) (Table 1).

Table 1. Summary of before (T0) and (T1) the treatment in each parameter (BP, sICAM and sVCAM)

Parameter	*T*0	*T*1	*P*
SBP (mmHg)	144 ± 19	129 ± 9	$P < 0.01$
DBP (mmHg)	93 ± 9	88 ± 8	$P < 0.01$
Proteinuria (g/24 h)	1.6 ± 0.7	1.1 ± 0.9	$P < 0.001$
sICAM (ng/ml)	628 ± 163	369 ± 112	$P < 0.001$
sVCAM (ng/ml)	1028 ± 649	688 ± 248	$P < 0.001$

SBP, systolic blood pressure; DBP, diastolic blood pressure; sICAM, soluble intracellular adhesion molecule-1; sVCAM, soluble vascular adhesion molecule-1.

Studies [2,4] have proven the important role of inflammation in the outcome of IgAN. Angiotensin type 1 (AT1) receptor antagonist significantly decreases proteinuria and slows renal deterioration in patients with IgAN. Our data suggest that treatment with irbesartan in patients with IgAN has a beneficial effect on inflammatory markers. The interfering with the inflammatory markers of AT1 antagonist could, at least partially, explain the effect of AT1 receptor blockade on renal survival in patients with IgAN. It is obvious that additional studies are needed to verify this hypothesis, especially in order to rule out the direct effect of lowering blood pressure on the inflammatory markers taken into consideration.

Conflict of interest statement. None declared.

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