The impact of Hypertension in Progression of Chronic Renal Failure

S. Plješa
Nephrological Department of Internal Clinic, Clinical Hospital Zemun-Belgrade

Arterial hypertension (HTA), the most common noninfectious disease of modern world, which exists in 10-25% of world population, represents a big chalenge for investigetors and doctors for a while now. The explanation for this interest is based on fact that HTA complications are multiple and multiorganic, among which kidney has an important role. It is known that hypertensive nephrosclerosis (HN), as an direct complication of HTA in kidneys in 25% of cases leads to end stage renal disease in USA and in 8% of cases in Europe. For the reasons mentioned, a great attention of researchers is directed to examining and explaining the relation between hypertension and kidneys.

Many studies have shown that it takes more years of hypertensive status before the fixed proteinuria appears as the first sign of kidney damage, followed by renal failure without any other primary kidney disease. Chronic renal failure caused by hypertensive nephroangiosclerosis most often appears around age of 65 years, while it is very rare in younger people around age of 45 years. This indicates that apart from present hypertension, age is of great importance in appearance of HN. The incidence of patients with mild artherial hypertension is 1:6000 patients in Europe and 1:2200 in USA.

Hypertensive nephrosclerosis, as a direct complication of HTA in kidneys, in great per-centage leads to end stage renal disease. The concept of glomerular ischemia is widely accepted as a primary lesion in HN, while many things are mentioned as other possible causes, such as genom which contributes in renal susceptibility for CRF, gene polimorphism which includes paracrine and autocrine agents which affect the endothelial and smooth muscle cells response to increased preassure and flow in afferent artheriol and their derranged response to increased Na^+ reach to macula densa.

It is considered that apart from hystological damages which are carracteristic for HN there are some other, such as myointimal hyperplasia of interlobular and afferent artheriola and hyalin arteriosclerosis specialy in affrent artheriola (1). These changes are a consequence of glomerular ischemia caused by shrinking of afferent artheriola. Shrinking of afferent artheriola leads to increased flow through the afferent artheriola causing extra myogen contractil response which is fol-lowed by tubuloglomerular feedback from macula densa which autoregulates glomerular capilary preassure and flow under physiological conditions. Destruction of nephrons within CRF causes a loss in autoregulatory abillity and transfer of systemic preasurre to glomerul, just as same as puls increase of glomerular volume during each heart beat.

It is supposed that changes in afferent artheriola such as colaps of basal membrane caused by schrinking and global sclerosis may be expected within excesive contraction of afferent artheriola that is followed by a great reduction of glomerular blood flow and preasurre. There are more and more data about endothelial cells demanding normal physiological level of shear stress caused by blood flow in order to avoid release of vasoconstrictors such as angiotensin II and endothelin in order to remain normal production of nitric oxid as vasodilatator. Low shear stress may increase susceptibility of endothelial cells to damage, may prevent apoptosis and lower response to cytokines.(2) Decreased blood flow through the afferent arteriol leads to intrarenal activation of renin-angiotensin-aldosteron system that leads to stimulation of cytokin TGF-β production that activates fibrosis processes.

High intake of salt is not only pathogenetic factor for essential hypertension but can also cause renal fibrosis throut increased production of TGF-β appart from its effect(3). Accordingly, excessive vasoconstriction most probably cause not only sodium retention and essential HTA but also contribute to development of HN.

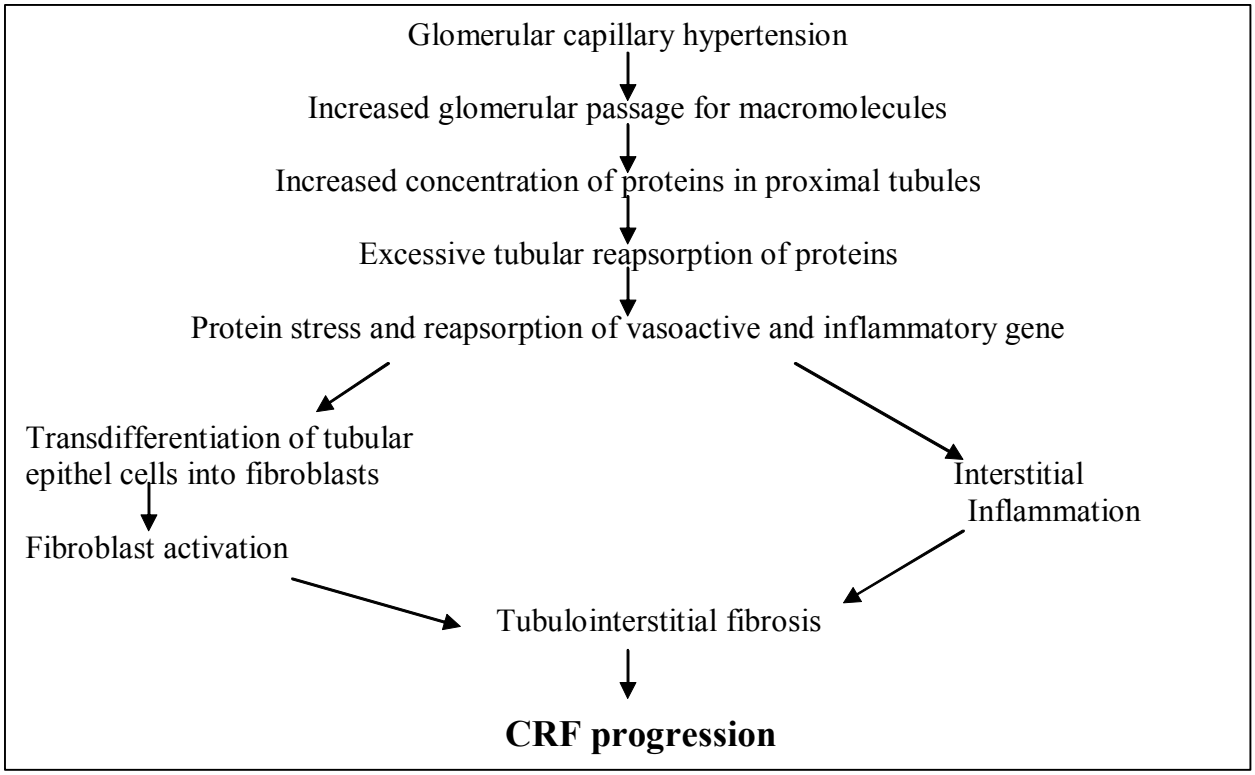
There is a need for identification of patients who will develop terminal CRF, possibly in reversible phase, out of large number of those with essential HTA. Potential predictors are black rase, eldery patients, positive family anamnesis for terminal CRF and avert microalbuminuria. It is shown that microalbuminuria significantly corelate with cardiovascular risk factors such as left ventricul hipertrophy, hiperlipidemia, increased preassure during nioght and increased diastolyc blood preasure (4). Although we can not say how microalbuminuria represent early HTA effect on glomerul and kidney function corellation of microalbuminuria with cardiovascular risk factors leads to intesive HTA therapy and blood preassure normalisation. It is possible that microalbu-minuria represent indicator of early changes in secundar focal glomerulosclerosis especialy if microalbuminuria show tendency of increasing.

It is evident that proteinuria represent the main pathophysiological mechanism of kidney damage in artherial hypertension. Proteinuria leads to glomerular and tubular damage causing nephron destruction which result in appearence of CRF (scheme 1).

If concept of primary glomerular ischemia is correct, logical conclusion may be that cal-cium antagonists could be anti

Correspondence to: Prof. Dr Steve Plješa, KBC Zemun –Belgrade, Vukova 9, 11080 Zemun, Serbia at Montenegro, Tel/fax.: ++ 381 11 3160282, E-mail: igma@verat.net

Scheme 1. Pathophysiology of kidney damage in artherial hypertension



hypertensives of first choice in HN treatment considering their ability to dilate afferent glomerular artheriola (5). Regulation of normal blod preassure is very important because it presents transmission of systemic preassure to glomerular capillary circu-lation.

In the last period combined usage of calcium antagonists and ACE inhibitors is consi-dered as a very reasonable solution. Calcium antagonists dilate afferent artheriola while ACE inhibitors inhibits and very efficiently prevent fibrosis and remodeling of preglomerular microvasculatura (6).

Other therapeutic procedures such as usage of AT-2 receptor blockers and gene therapy are possible. Data about first experiments with gene therapy in HTA and HN are very interesting. They led to fascinating results of calicrein and NO gene usage in experimental animals (7). How will the growing knowledge in area of genetics and positive and negative effect of gene therapy bne applicated is still to be seen in new millenium.

References

1. Kashgarian M. Hypertensive Disease and kidney Structure. In: Laragh JH and Brenner BM eds. Hypertension:Pathophysiology, Diagnosis and Management, Second Edition, Raven Press, Ltd., New York: 1995:433-443.
2. Braddock M, Schwachtgen JL, Houston P, Dickson MC, Lee MJ, Campbel CJ. Fluid shear stress modulation of gene expression in endothelial cells.News Physiol Sci1998; 13: 241-246.
3. Ying W, Sanders PW. Dietary salt modulates renal production of transforming- grow factor-β in rats. Am J Physiol 1998; 274 (Renal Physiol, 43): F635-F641
4. Pontremoli R, Viazi F, Sofa A et al. Microlabuminuria: A marker of cardiovascular risk and organ damage in essential hypertension. Kindney Int 1997; 52(Suppl): S163-S165.
5. Mene P. Calcium channel blockers: what they can and what they can`t do. Nephrol Dial Transpl 1997; 12: 25-28.
6. Skov K, Fenger-Gron J, Mulvany MJ. Effects of an angiotensin-converting enzyme inhibitor, a calcium antagonist, and an endothelin receptor antagonist on renal afferent arteriolar structure. Hypertension 1996; 28: 464-471.
7. Lin KF, Chao L, Chao J. Prolonged reduction of high blood pressure with human nitric oxide syntheses gene delivery. Hypertension 1997; 30(I): 307-313