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Review

Chronic kidney disease and ageing

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In recent decades, life expectancy has significantly extended, and the number of elderly people in each population increases significantly during the subsequent years. Ageing is associated with a physiological deterioration of kidney function, however, in patients with additional diseases such as diabetes, hypertension and obesity, there is often stronger severity of kidney damage. It has been estimated that the prevalence of chronic kidney disease (CKD) in the older population is several times higher than in the general population. It is considered that in addition to the mentioned above comorbid the socio-economic factors also increases prevalence of CKD. The occurrence of CKD significantly increases the mortality, deteriorating the quality of life of these subjects and is also severe financial problem for the health care system because of the high costs of renal replacement therapy. For this reason, renal replacement therapy in elderly patients is expensive and not always brings measurable benefits.

Key words: Chronic kidney disease, Ageing, Renal replacement therapy

INTRODUCTION

In recent decades, life expectancy has significantly increased and it seems that this trend will be maintained, which will result in constantly growing number of elderly people in coming years [1]. It has been estimated that in 2030 in the United Kingdom the average life expectancy of women will be 91 years and men 88 years [2]. Even though the ageing is a physiological process, the prevalence of diseases in group of elderly people is much greater than in general population. It has been shown that a 75 years old person statistically suffers from 3 or more diseases [3]. Interestingly, only 5% of people over the age of 75 in the United States in 2005 had no health visits [4]. Chronic kidney disease (CKD) is one of the diseases, which is characterized by increasing incidence with ageing. It has been shown that in the United States the prevalence of CKD is from 11% in general population and up to 30% among elderly persons [5]. The occurrence of CKD significantly increases the risk of death in elderly patient with diabetes, hypertension, heart disease or stroke. CKD also reduces life quality [6] by increasing risk of occurrence depression [7] functional losses [8], frailty [9], falls and fall-related injuries [10 11], hospitalization and loss of independence [12] and cognitive decline [13]. Chronic kidney disease–generates also a significant costs to the health care system. It has been estimated that if dialysis is necessary, the average annual cost of treatment is from 70 thousand USA dollars in the patients aged 60-64 years to over 86 thousand USA dollars in patients over 85 years of age [14]. Taking into account the above-mentioned aspects it is important to pay special attention to this problem, because early diagnosis and treatment can improve survival, quality of life and reduce total cost of treatment [15].

PATHOMECHANISM OF CHRONIC KIDNEY DISEASE IN ELDERLY

Changes that occur in the kidney during ageing can be divided on two parts namely: structural and functional. Structural changes include: decreased kidney weight

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and volume; glomerulosclerosis; cortical atrophy and loss of renal parenchyma; capillary tuft collapse; increased glomerular basement membrane (GBM); deposition of hyaline in GBM; change in GBM composition; interstitial fibrosis; tubular atrophy; intrarenal arteriosclerosis; thickened intima and obliteration of afferent and efferent arterioles [16 17]. An autopsy study has shown that the number of glomeruli per kidney ranges from 250,000 to 1.5 million at birth and after the age of 18 the reduction of that number takes place with is about 6,752 glomeruli per year [18]. Other studies have shown a reduction in the weight of kidneys during the process of ageing from over 400g in 3rd and 4th decade to less than 300g in the 9th decade [19]. Denic et al. have analyzed 1638 living kidney donors. It has been shown that donors aged 18-29 years had a mean 990,661 non-sclerotic glomeruli per kidney in comparison with 520,410 non-sclerotic glomeruli in donors aged 70-75 years [20]. It also has been shown that the number of completely sclerotic glomeruli in the group of elderly donors was more than 8 times higher. Other analysis of 1046 biopsy samples from donors has shown an increase in the percentage of sclerotic glomeruli with age [21]. The above mentioned changes lead to the loss of functional glomeruli and progression of CKD.

The functional changes in the kidney resulting from ageing include: decreased glomerular filtration rate (GFR); decreased effective renal plasma flow (ERPF); increased filtration fraction (FF); increased reno-vascular resistance (RVR); impaired water, electrolyte, and glucose handling; decreased diluting and concentrating capacity; renal vasoconstriction; decreased plasma renin activity and aldosterone; increased tissue angiotensin II and endothelin and decreased vasodilator activity of prostacyclin [16]. It is estimated that the average physiological reduction in eGFR per year is about 0.68 mL/min/1.73m^2 in men and 0.68 mL/min/1.73m^2 in women [22]. In individuals older than 40 years of age, eGFR decreases by about 1 mL/min/1.73m^2 per year. Decline in ERPF after that age is about 8 mL/min/1.73m^2 [23]. Another study has shown decline in eGFR about 1.05 mL/min/1.73m^2 in individuals aged 70-110 years [24]. The proposed mechanisms for ageing-associated renal disease are: oxidative stress; telomere shortening and loss off mitochondria; intrarenal activation of the renin angiotensin system; endothelial dysfunction; renal ischemia; increased renal TGF-β expression; accumulation of advanced glycation end products (AGEs) and chronic effects of uric acid.

EPIDEMIOLOGY OF CHRONIC KIDNEY DISEASE IN THE ELDERLY

Chronic kidney disease is a major and growing health burden in Europe. One in 3 Europeans is at an increased risk of developing CKD. A striking 1 in 10 already has impaired kidney function severe enough to affect their health status. The current rise in diabetes, obesity and ageing will further worsen this situation unless there is greater focus and concerted action by European health policy-makers. Large population studies in different countries have shown that the prevalence of CKD range from 7% to more than 18% [25]. It has been estimated that the average prevalence of CKD in the world increases with age and reaches almost 30% of individuals over 70 years of age [26]. Impaired renal function (eGFR less than 60 mL/min/1.73m^2) in group of individuals aged over 80 years occurs from 18,6% to over 50% [27]. The Polish population study PolNef involving almost 2,500 participants has shown that the frequency of CKD is 18.6%. Almost 12% of studied population have albuminuria. Interestingly, it has been shown that nearly 70% of patients with CKD have also hypertension [28-30]. The first polish multidisciplinary study of the elderly population PolSenior, which involve 5695 participants has shown that the prevalence of CKD in this group is nearly 30%. In group of individuals aged over 90 years CKD occurs in over 60% [31]. Interestingly, only 3% of subjects with CKD were aware of the presence of kidney disease. The study has shown the coexistence of CKD with diabetes, hypertension, prostatic hyperplasia, heart failure, coronary artery disease, the occurrence of myocardial infarction and stroke. Socioeconomic aspect also affects the incidence of CKD. It has been shown slightly higher incidence of CKD in the rural population, among people non-smoking and non-consuming alcohol. Crews et al. in observational study has shown a significantly higher prevalence of CKD among African Americans with lower socioeconomic status [32]. Such a correlation was not found in caucasians. Also, other studies have shown the negative impact of socioeconomic status on risk for CKD [33]. In the REGARDS Study it has been shown that lower income is an independent risk factor for mortality in patients with CKD [34]. Factors that combine low socioeconomic status with chronic kidney disease is certainly health-related behaviors like intensive alcohol intake, cigarette smoking, diet, physical activity, sedentary time; co-morbid conditions and access to healthcare [35].

RENAL REPLACEMENT THERAPY IN ELDERLY PATIENTS

The most common method of treatment of end-stage renal disease is renal-replacement therapy (RRT). It is known that starting hemodialysis treatment in elderly patients with CKD does not always bring measurable benefits. It has been shown that in elderly CKD patients without ischemic heart disease and extensive comorbidities RRT extends the lives [36-38]. Unfortunately mentioned above advantage is often associated with the deterioration of the quality of life, due to, among others, large number of hospitalizations [3]. Furthermore, it has been shown that initiation of hemodialysis therapy in the oldest group of patients (aged over 80 years) is associated with more than 50% mortality during the first year of treatment [6]. As it was mentioned above, the cost of renal replacement therapy in older patients reach over 86 thousand USA dollars per year [14]. The age of patients treated with RRT is steadily increasing. Incidence of dialysis therapy during last 10 years is decreasing but that of pre-emptive transplantations is clearly on the rise (more than doubled over last 10 years) [39]. It is important because the life expectancy of dialysis patients is reduced by two thirds compared with the general population and that of transplant recipients by 25-30% [40].

CONCLUSIONS

Comorbidities and lifestyle often exacerbate the physiological ageing process of kidney. CKD occurs frequent in elderly population and its prevalence range from 30 to 40% of individuals. Considering the ageing of the population and the increasing prevalence of diabetes, hypertension and obesity it seems that the incidence of CKD will be increasing in coming years. The prophylaxis and treatment of CKD should take into account potentially modifiable factors like health-related behaviors, comorbid conditions, and health-care access. It should be noted that lower socioeconomic status might lead to poorer self-management and thus greater complications from systemic disorders like diabetes or arterial hypertension. Socioeconomic factors seem to be a suitable target for interventions at the national and supranational level aimed at reducing disparities in CKD. The age of patients treated with renal replacement therapy is steadily increasing. It should be remembered, however, limited benefits of renal replacement therapy in the group of oldest CKD patients.

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